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SEPTICEMIA IN THE NEW-BORN

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Septicemia in the new-born, although undoubtedly not so frequent as before the introduction of aseptic obstetric technic, still plays an important and often unrecognized rôle in neonatal morbidity and mortality. Even at the present time, however, no data are available on its true incidence because of the relative infrequency with which blood cultures of young infants are made. Many cases of septicemia are overlooked or are diagnosed only when localized lesions appear unless blood cultures are made in all cases of obscure illness in the neonatal period.

The present report of thirty-nine cases of septicemia in the new-born seen in the wards of the New Haven Hospital illustrates the frequency with which such diagnoses can be made if routine blood cultures are made as an aid to diagnosis in this period of life.

REVIEW OF THE LITERATURE

Only eight reports of streptococcus septicemia in the neonatal period confirmed by blood cultures have been found. All of these cases had a fatal termination.

De Lange [1] described an infant who on the third day of life became jaundiced, after which signs of extrapyramidal motor disturbance developed. A blood culture made on the twenty-sixth day showed hemolytic streptococci. The author considered this a case of "sepsis neonatorum" of umbilical origin, with jaundice and injury to the nuclei of the brain. Browne and Kincaid [2] reported "hematogeneous streptococcal infection" of the fetus of a clinically healthy mother. The fetus was macerated, and a culture from the heart's blood showed streptococci. Rosenbaum [3] described cases of a morbiliform eruption in young infants

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1. de Lange, C.: Extrapyramidale Bewegungstörung bei Sepsis Neonatorum, Acta pædiat. **4**:60, 1925.

2. Browne, W. H., and Kincaid, H. L.: Etiology and Diagnosis of Intra-Uterine Fetal Death, J. A. M. A. **87**:847 (Sept. 11) 1926.

3. Rosenbaum, S.: Ueber Morbiliforme Neugeborenengrippe mit septischen Ausgang, Monatschr. f. Kinderh. **43**:153, 1929.

having a "septic outcome" (*septischen Ausgang*). Two of these infants had a hemolytic streptococcus septicemia proved by blood culture, in one on the sixth and in the other on the thirty-sixth day of life. Fonteyne, Millet and Verhoogen [4] reported the case of a 4 weeks old infant with cutaneous lesions from which streptococci were grown. A blood culture on the day of death showed streptococci. At autopsy streptococcus meningitis was found to be present. Campbell [5] reported three cases of septicemia in infants under 1 month of age. Hemolytic streptococci were isolated in pure culture from the blood during life. These cases were complicated by osteomyelitis, meningitis and peritonitis. All three infants died.

Staphylococcus, Bacillus coli and pneumococcus septicemia have also been infrequently reported.

Castle [6] reported the case of an infant in whom cutaneous lesions developed at the age of 9 days. When seen at the age of 18 days he had multiple abscesses and otitis media. Cultures from the abscesses showed staphylococci, and a pure culture of staphylococci was isolated from the blood on two occasions. The infant recovered and was discharged as well at the age of 7 weeks. Laffont and Mélé [7] described a case of staphylococcus septicemia in a woman who was delivered of a premature infant. The infant died about one-half hour after birth, and a culture of blood obtained by heart puncture showed staphylococci. The mother's blood culture two days before delivery showed staphylococci. Vaglio [8] observed many cases of sepsis of the new-born in an infants' asylum. The cases were said to have been anatomically, bacteriologically and histopathologically verified as instances of true sepsis. Diplococci and staphylococci were isolated from the blood even before the final stage. In one case Bacillus pyocyaneus was demonstrated.

Condat [9] cited the case of a 10 day old infant in whom fever and convulsions developed; the child died on the sixteenth day. A culture of blood taken by heart puncture showed B. coli. Cultures from the pericardial fluid showed pneumococci.

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4. Fonteyne, Millet and Verhoogen, Robert: Deux cas de septicémie à streptocoques chez des nourrissons, Méd. inf. **35**:113, 1929.

5. Campbell, L. A.: Septicaemia in Children, Canad. M. A. J. **24**:674, 1931.

6. Castle, W. F.: Multiple Subcutaneous Abscesses in Infants, Brit. J. Child. Dis. **22**:122, 1925.

7. Laffont and Mélé: Passage du staphylocoque par voie placentaire au cours d'une staphylocociémie hortelle avec méningite, Bull. Soc. d'obst. et de gynéc. **15**: 566, 1926.

8. Vaglio, R.: Contribution to a Study of Sepsis of the Newly Born Infant, Pediatria **36**:1, 1928.

9. Condat: Sur une petite épidémie de pneumococcie chez le nouveau-né, Arch. de méd. d. enf. **20**:88, 1917.

Condat [9] also reported the case of an infant who died on the fifth day of life. A blood culture made from heart's blood showed pneumococci.

Voigt [10] has reported a case of paratyphoid B. septicemia, and Henschen and Reenstierna [11] a case of B. proteus septicemia in new-born infants. In both cases the organisms were found in the blood post mortem.

REPORT OF CASES

A diagnosis of septicemia of the new-born has been made on the basis of positive blood cultures in thirty-nine infants admitted in a period of five years to the wards of the New Haven Hospital. Since the chief interest in reporting these cases centers around the bacteriologic evidence of generalized infection, the cases have been divided for study into five groups according to the organisms found in the blood cultures. In group I are fifteen cases of streptococcus septicemia; in group II, eleven cases of staphylococcus septicemia; in group III, ten cases of B. coli septicemia; in group IV, two cases of pneumococcus septicemia, and in group V, one case in which B. pyocyaneus was isolated from the blood stream. Not only will the bacteriologic findings be described for these five groups, but it will be pointed out how the clinical symptoms, prognosis and source of infection vary with the type of invading organism.

The clinical histories in the thirty-nine cases included in this study are given in detail in the abstracted case reports at the end of the paper.

Comment on Clinical Data.—Of the thirty-nine cases of septicemia, thirty occurred in boys and nine in girls, which indicates a striking predominance among boys. All of the infants reported on were less than 1 month old when the illness began. Symptoms were present at birth in eight cases; they appeared on the first day of life in four cases, during the first week in nineteen cases, during the second week in nine cases and later than the second week in eight cases. In twenty-eight of the thirty-nine cases the symptoms appeared during the first two weeks of life. In three the onset was indefinite but occurred before the end of the first month of life. No relation could be shown between the age at the onset of symptoms and the type of organism isolated from the blood stream.

The first evidences of illness were manifold and as a rule suggested rather that the infant was acutely ill than that septicemia might be the

10. Voigt, O.: Beobachtungen von Paratyphus-B-Erkrankungen bei Neugeborenen, Monatschr. f. Kinderh. **23**:23, 1922.

11. Henschen, F., and Reenstierna, J.: Zur Pathogenese der sogenannnten weilchen Krankheit: Ein Fall von Proteus Infektion beim Säugling, Ztschr. f. Kinderh. **14**:185, 1916.

cause of the illness. The incidence of general symptoms of illness and of clinical evidences of localized infection for the five bacteriologic groups have been summarized and are shown in table 1. It should be noted that the various symptoms and evidences of infection were not always recorded. The number of cases in which no record was made is indicated in the table, as well as the number showing the presence or absence of the symptoms on examination. Study of this table and of the individual case records brings out a number of points of clinical interest.

Fever was present during the course of the illness in thirty-three cases. No characteristic temperature curve was found; a "septic" type

TABLE 1.—*Evidences of Infection*

	Groups According to Organisms												
	Strepto-coccus (15 Cases)		Staphylo-coccus (11 Cases)		B. Coli (10 Cases)		Pneumo-coccus (2 Cases)		B. Pyo-cyaneus (1 Case)		Total		
Signs	Pres.	Abs.	Pres.	Abs.	Pres.	Abs.	Pres.	Abs.	Pres.	Abs.	Pres.	Abs.	No Report
Generalized													
Fever	13	1	10	1	7	1	2	0	1	0	33	3	3
Enlarged spleen	5	7	8	3	5	4	1	1	0	1	19	16	4
Jaundice	0	13	7	4	6	4	0	2	1	0	14	23	2
Bleeding	0	14	5	6	3	7	1	1	1	0	10	28	1
Leukocytosis W.B.C. over 20,000	5	6	5	5	2	6	0	0	1	0	13	17	9
Anemia R.B.C. less than 5,000,000	8	2	1	8	6	2	0	0	0	1	15	13	11
Hemoglobin less than 100 per cent	7	2	3	6	5	1	0	0	0	0	15	9	15
Localized													
Cutaneous lesions	12	3	5	6	1	9	0	2	0	1	18	21	0
Omphalitis	5†	8	1*	10	1*	9	0	2	0	1	7	30	2
Meningitis	4	11	3†	8	1*	9	1	1	0	1	9	30	0
Osteomyelitis	1	14	1	10	1	9	0	2	1	0	4	35	0
Peritonitis	4	11	1*	10	3†	7	0	2	0	1	8	31	0
Otitis media	7	8	1	10	0	10	1	1	0	1	9	30	0
Pyelonephritis	0	15	0	11	3	7	0	2	0	1	3	36	0

* One diagnosis made post mortem only.
† Two diagnoses made post mortem only.

of curve was unusual. In one case (staphylococcus septicemia) the temperature was normal throughout the course of the disease; in three cases the temperature was not taken, and in two cases subnormal temperatures were found in infants who were moribund on admission.

Although enlargement of the spleen is commonly considered to be evidence of generalized infection, it was found in only nineteen of the thirty-nine cases of septicemia.

Jaundice occurred in fourteen of the thirty-nine cases reported and was severe in twelve. It was present at birth in four cases and appeared before the eighth day in nine, and the time of its appearance was not recorded in one case. Jaundice occurred frequently in the cases of staphylococcus and B. coli septicemia, and was present in the case in

which B. pyocyaneus was isolated. It was not observed, however, in any of the cases of streptococcus or in the two cases of pneumococcus septicemia.

Although bleeding has commonly been considered a manifestation of septicemia of the new-born, it was found only ten times in the thirty-nine cases, and never in the group with streptococcus septicemia. Bleeding occurred twice in the skin, once from the urinary tract, once from the nose, once from the nose and mouth and four times from the gastro-intestinal tract. In one case bleeding occurred not only from the gastro-intestinal tract but from the nose and into the submucosa of the palate.

White blood cell counts made in thirty cases on admission gave results varying from leukopenia, with from 4,000 to 5,000 cells, to leukocytosis with from 30,000 to 50,000 cells. There seemed to be no relation to the type of organism found in the blood stream, leukopenia as well as leukocytosis occurring in infants in each of the three chief bacteriologic groups. It is of interest to point out, however, that all of the infants with leukopenia died, as did four infants with counts of over 30,000. In five infants who survived, the counts ranged between 10,000 and 20,000. The differential white counts also varied greatly, though leukocytosis of the polymorphonuclear type occurred more often than that of the lymphocytic type.

Red blood cell counts were made in twenty-eight cases. In five cases only was the count under 4,000,000, and in ten cases it was between 4,000,000 and 5,000,000. In two cases there was progressive anemia, the red cell count dropping as low as 1,100,000 and 1,270,000 respectively. From table 1 it can be seen that anemia was more frequent in streptococcus and B. coli septicemia than in staphylococcus septicemia.

Signs of localized infection were found in thirty of the thirty-nine cases reported, nineteen showing two or more foci. The total incidence of these signs is shown in table 1, as well as the frequency with which they occurred in each of the five bacteriologic groups.

Localized cutaneous infections were much more common in the streptococcus group than in any of the other groups. Nine infants with streptococcus septicemia had erysipelas, two had localized abscesses, and one an infection at the site of a congenital defect in the abdominal wall. In five cases of staphylococcus septicemia there were definite cutaneous infections. Pemphigus was present in one case and dermatitis exfoliativa in one, and in three cases multiple abscesses developed which were probably the result rather than the cause of the infection in the blood stream. In one case of B. coli septicemia there was a cutaneous infection following a severe burn.

Of the seven cases of omphalitis, three showed clinical evidence of infection of the umbilicus, and in four the diagnosis was made only at postmortem examination.

A diagnosis of meningitis was made clinically in six cases. Cultures of the spinal fluid showed streptococci in four cases and staphylococci in one case, and there was a mixed culture (pneumococcus, staphylococcus and B. coli), classified in the pneumococcus group, in one case. The organisms found in the spinal fluid were the same as those isolated from the blood in all of these cases. Meningitis was found at postmortem examination in three additional cases, two due to the staphylococcus and one to B. coli.

Osteomyelitis occurred only four times. In one case of streptococcus septicemia, mastoiditis was found post mortem. Many bones were involved in one case of staphylococcus septicemia. Osteomyelitis of the humerus occurred in one case of B. coli septicemia, and osteomyelitis of the clavicle in the one case of pyocyaneus septicemia. A clinical diagnosis of osteomyelitis was made in the last three cases, and the diagnosis was confirmed by roentgen examination in two of these and at operation in one. Osteomyelitis did not occur in the two cases of pneumococcus infection.

Peritonitis was found clinically in five cases, and the diagnosis was confirmed at postmortem examination in three of these. It was also found post mortem in three cases in which it was not suspected clinically. In two cases peritonitis was the result of perforation of gastric ulcers.

Otitis media occurred in nine of the cases of septicemia. It was present in seven cases on admission, being suppurative in two of these. In two cases otitis media developed during the course of the illness. Otitis media occurred most frequently in streptococcus septicemia.

Evidences of infection of the urinary tract were present in three cases. Two of the infants died, and at postmortem examination suppurative nephritis was found in both cases. One infant survived who was thought to have a congenital malformation of the urinary tract with superimposed infection. All three infants had B. coli septicemia.

Data on Blood Cultures.—Since the diagnosis of septicemia in the cases reported was based ultimately on the finding of organisms in the blood, the results of blood cultures are reported in detail.

As already stated, the cases were divided into five groups according to the organisms found in the blood cultures. The number of blood cultures made and the results are shown in table 2. The day of life on which the culture was made is shown, as well as the result of the culture, stated as + or 0, indicating the presence or absence of organisms. In each case the upper sign relates to broth cultures, and the

TABLE 2.—*Results of Blood Cultures**

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Group I. Streptococcus

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
1	— J.		2 days died	+
				—
2	— B.		5 hours died	+
				—
3	— B.		15 days died	+
				—
4	R. T.	23	23 days died	
		+		
		+		
5	R. R.	22	25 days died	+
		0		+
		—		
6	T. C.	16 32 33	34 days died	
		0 + +		
		0 + +		
7	R. L.	8	9 days died	+
		+		—
		+		
8	R. W.	28	32 days died	+
		+		—
		+		
9	P. D.	28	36 days died	
		+		
		+		
10	J. B.	13 15 16	17 days died	
		0 + +		
		0 0 0		
11	M. S.	42	44 days died	
		+		
		—		
12	C. F.	26	27 days died	
		+		
		—		
13	J. W.	33	35 days died	+
		0		+
		+		
14	A. G.	40	47 days died	+
		+		+
		—		
15	D. N.	7	8 days died	
		+		
		—		

Group II. Staphylococcus

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
16	R. T.	3 5 6 16 19 21 25 26 28 30 40	2 years living	
		+ 0 0 — 0 0 0 0 0 0 0		
		+ 0 — 0 — 0 0 0 — — 0		
17	G. W.	13 17 19 21 25 27 28 30 4 mo.	5 years living	
		0 0 0 + + — 0 0 0		
		— — — + — + 0 0 0		
18	D. G.	20 23 43 46	3 months died	
		+ + + 0		
		— — — —		
19	E. T.	40 42	42 days died	
		+ —		
		— +		
20	A. S.	3 4	5 days died	+
		0 0		+
		0 —		
21	— L.	2 4 6 9 11 15 17 22 25	2 years living	
		+ + + + 0 + 0 0 0		
		+ + — — 0 + — 0 0		
22	— B.	4	4 days died	+
		+ 0		+
		0 0		
23	R. J.		30 days died	+
				—
24	J. M.	11 13 15 23	30 days died	+
		+ + 0 +		—
		+ — 0 —		
25	R. Z.	18 21	21 days died	
		+ +		
		— —		
26	H. A.	19	19 days died	
		+		
		+		

Group III. B. Coli

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
27	S. H.	29 30 34 35 43 48 54 61 69 70	6½ years living	
		+ 0 + + 0 0 0 0 0 0		
		— — — — — — — — — —		
28	J. R.	28	28 days died	+
		+		—
		—		
29	N. S.	4 6 9 14 16 17 18	21 days died	
		+ + 0 + + + +		
		— — — — — — —		
30	F. M.	3	3 days died	
		+		
		—		
31	G. G.	2 15 17 18 21 22	25 days died	+
		0 + 0 + + +		+
		0 + — + — —		
32	— G.	1	20 hours died	
		+		
		+		
33	— B.		2 days died	+
				+
34	— L.		10 days died	+
				—
35	D. H.	16 19 25 31 33 41	52 days died	
		0 0 + + + +		
		— — + — — —		
36	G. S.	11 16 24 26 30 38 49	6 months living	
		+ + 0 0 0 0 0		
		+ 0 0 — — — —		

Group IV. Pneumococcus

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
37	P. F.		2 days died	+
				—

Pneumococcus and Staphylococcus and B. Coli

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
38	G. P.	18	18 days died	
		+		
		+		

Group V. Pyocyaneus and Staphylococcus

No.	Name	Day of Life and Result of Blood Culture	Outcome	Post-mortem Blood Culture
39	J. B.	15 20 25	26 days died	0
		+ + 0 0		—
		— — —		

* The figure refers to the day of life on which the blood culture was taken. The upper row of symbols refers to broth cultures. The lower row of symbols refers to plate cultures. + = positive culture. 0 = negative culture. — = culture not made.

lower to plate cultures. A dash (—) above or below indicates that the broth or the plate culture was not made.

In group I were fifteen cases of streptococcus septicemia; in fourteen the organism was hemolytic, and in one nonhemolytic. The diagnosis was made on the basis of a single positive culture in nine cases, in five before and in four after death. In only two cases in this group were repeated cultures made ante mortem because, as a rule, death occurred soon after the patient's admission to the hospital. In four cases single cultures, positive before death, were verified by cultures after death. In eight cases broth and plate cultures were both positive, in seven cases broth cultures only were positive.

In group II were eleven cases of staphylococcus septicemia. In contrast to group I, many repeated blood cultures were made in this group. Single cultures were made in only two cases, while in the other nine a total of forty-eight cultures were made. The diagnosis was based on a single positive culture in four cases, in two ante mortem and in two post mortem. In three of these cases (cases 16, 20 and 26) the organisms were found both in broth and in deep colonies in plates; in the fourth case (case 23), although organisms were found in broth alone in a culture made post mortem, the presence of deep metastatic abscesses from which staphylococci were grown justified the diagnosis of septicemia on inadequate blood culture findings. In seven cases the diagnosis was based on two or more positive blood cultures. Three infants in this group (cases 16, 17 and 21) recovered, and all had three or more negative blood cultures before discharge from the hospital.

In group III were ten cases of B. coli septicemia. The diagnosis was based on a single positive culture in four cases, in two ante mortem and in two post mortem. In six cases the cultures were positive on two or more occasions. In two cases cultures positive during life were positive post mortem also. Two infants in this group survived. In one case, three positive cultures were followed by five negative cultures; in the other, two positive cultures were followed by six negative ones before the patient's discharge from the hospital.

In group IV were two cases, one due to the pneumococcus, and the other to a mixed infection with pneumococci, staphylococci and B. coli. In the first case, a culture of blood taken post mortem by heart puncture showed a pneumococcus (group IV). The possibility of contamination of the needle as it passed through the lung must be considered. No signs of pneumonia were present, but postmortem examination was not made. In the other case, included in this group because pneumococci grew in the culture, staphylococci and B. coli were also present. All three organisms grew in broth cultures and also in poured plates, the blood being taken during life. These three organisms were also found in cultures made from pus from an abscess of the cheek.

In group V was one case in which B. pyocyaneus and staphylococci were both grown in two broth cultures taken six hours apart on the fifteenth day of life. The infant was repeatedly given transfusions, and three subsequent cultures were negative.

Altogether, blood cultures were positive ante mortem in thirty cases, and post mortem only in nine cases. Blood cultures positive during life were confirmed by postmortem cultures in seven cases.

Criteria for Bacteriologic Diagnosis.—To interpret blood cultures correctly is sometimes difficult since the presence of organisms in the cultures may be the result of cutaneous or other contamination rather than evidence of true infection in the blood stream. In the case of postmortem blood cultures there is danger not only of contamination from the skin and other tissues but also of postmortem invasion of the blood.

When aseptic technic is used and the blood is readily obtained, the presence of streptococci or of B. coli in blood cultures made during life, whether in broth or in plate cultures, has been considered as definite evidence of infection of the blood stream, since neither of these organisms is ordinarily found as a contaminant.

On the other hand, the presence of staphylococci in blood cultures is less easy to interpret, because these organisms are commonly found on the skin and may appear as laboratory contaminants.

Because of the difficulty in interpretation of the significance of staphylococci in blood cultures, a special study of a series of forty-nine normal new-born infants was made. One hundred and fifteen blood cultures were made.[12] In all of the cultures broth was used; in seventy-two, poured plates also were made. Of the one hundred and fifteen broth cultures, seventy-six (66 per cent) were negative and thirty-nine (34 per cent) were positive. In the positive broth cultures Staphylococcus albus was found thirty-five times and Staphylococcus hemolyticus, Staphylococcus aureus, diphtheroids and a green streptococcus once each.

Of the seventy-two plate cultures, fifty-five (76 per cent) were negative, while seventeen (23 per cent) were positive. In the plate cultures Staphylococcus albus was found thirteen times and hemolytic staphylococci three times, associated once with a nonhemolytic staphylococcus, and in one case the type of organism was not determined. Cultures were twice positive in five cases. The organism in four of them was Staphylococcus albus. A growth was present in both broth and plate cultures in three of these four cases, but the colonies in the plate cultures were few. In the fifth case a culture showed Staphylo-

12. Drs. E. Gordon, H. Harrison, P. Harper and V. N. Lippard made the cultures for this study.

coccus aureus in broth but Staphylococcus albus on the plate, and when the culture was repeated Staphylococcus albus was found in broth and the plate showed no growth. In all five cases cultures from the skin showed Staphylococcus albus. The number of cultures in which contaminants were found varied widely (between 20 and 50 per cent) in the hands of the four persons who did the venous punctures and inoculated the cultures.

Skin cultures were made in sixty-nine cases after the skin had been cleaned with iodine and alcohol prior to the venous puncture. In forty, or 58 per cent, of the cases the culture was positive. Staphylococcus albus was found in thirty-eight cases, in one of which it was associated with a gram-positive bacillus.

From this study it seems justifiable to conclude that Staphylococcus albus is found frequently and other organisms occasionally as contaminants in cultures made from the blood of apparently healthy infants. If they occur in one culture alone, or in broth and not in plates or as superficial colonies on plates, the organisms are usually contaminants.

In the thirty-nine cases of septicemia reported in this paper a diagnosis of staphylococcus septicemia was not made unless the organisms were found in repeated broth cultures or in deep colonies on plates, or in both broth and plates in single cultures, except in one case (case 23) in which multiple deep abscesses were present from which staphylococci were grown.

In postmortem cultures organisms were considered as positive evidence of antemortem infection of the blood stream only when the cultures were made by heart puncture immediately after death and if the organisms were found in deep colonies in plates as well as in broth cultures. Ylppö [13] accepted as evidence of septicemia organisms grown from blood obtained by heart puncture immediately after death in twelve of twenty-nine premature infants.

In the thirty-nine cases of septicemia reported here a total of one hundred and twenty-four cultures were made, twenty-four in group I, fifty in group II, forty-three in group III, two in group IV and five in group V. Pure cultures were obtained in all but eight cases. In group I staphylococci as well as streptococci were found in two of twenty-four cultures. In group II, in fifty cultures made two showed organisms

13. Ylppö, A.: Pathologisch-anatomische Stüdien bei Frühgeborenen, Ztschr. f. Kinderh. **20**:371, 1919. The organisms found were B. coli six times, staphylococci three times, streptococci once and unidentified organisms twice. The finding of B. coli in one half of the cultures was considered by Ylppö to be evidence that in premature infants the gastro-intestinal tract is a frequent portal of entry for organisms into the blood stream. He cited DeLestre, on the other hand, as favoring the respiratory tract as the most important portal of entry for infection of the blood stream in the premature infant. The latter, in 1901, reported finding bacteria fifteen times in nineteen cases, in five of which B coli was the organism.

other than staphylococci. In group III, in forty-three cultures made four showed organisms other than B. coli. In group IV, a pure culture was obtained in one case, and in the other, although three organisms were found, the same organisms were found in a culture made from an abscess of the cheek. In group V staphylococci were found with B. pyocyaneus in all cultures made.

Portal of Entry or Source of Infection.—The exact portal of entry or source of the infection of the blood stream in these cases is often difficult to determine. In some cases no source can be determined; in others a conjecture only can be made, while in others several sources are possible.

In the thirty-nine cases of septicemia reported, a hematogenous source was suspected in eight cases, in three of which (cases of streptococcus septicemia) the mother's blood culture also showed streptococci. In seven cases the mother's membranes ruptured prematurely. In five of these cases the infants had staphylococcus, in one case streptococcus and in one case B. coli septicemia. Umbilical infection, present in seven cases, was due to the streptococcus in five, to the staphylococcus in one and to B. coli in one. Cutaneous infection was present in fifteen cases, in eight of which the lesion was erysipelas. Three infants had other severe cutaneous lesions, one dermatitis exfoliativa, one a congenital defect of the abdominal wall with infection and the third an abscess of the cheek. Two infants had infections following circumcision, and one following an insect bite on the hand. Three infants had infected lesions of the mouth; seven had diarrhea, and three had suppurative otitis media.

In six of the cases of septicemia there was no obvious source of infection; in twenty-eight cases there was only one source, and in five cases several possible sources of infection were present.

Ten of the mothers were ill at the time of delivery of the infant or had a febrile puerperium. Four mothers had septicemia, two, thrombophlebitis one, grip, and one, pyelitis and nephritis which was fatal. Two mothers had unexplained fever during the puerperium.

Treatment.—In the treatment of infants with septicemia transfusions of blood are undoubtedly extremely important. Subcutaneous injections of physiologic solution of sodium chloride (hypodermoclyses) are useful to prevent or combat dehydration when fluids are being lost by vomiting and diarrhea or when fever is present. Intravenous injections of dextrose also seem to be beneficial in many of these cases. Transfusions, hypodermoclyses and intravenous injections of dextrose solution were repeatedly given in many of the cases reported.

Altogether, two hundred and twenty-nine hypodermoclyses were given to twenty-one infants, ninety-five transfusions of blood to twenty-six

infants and twenty-six intravenous injections of dextrose solution to twelve infants. The greatest number of transfusions given to any one infant was fifteen; the greatest number of intravenous injections of dextrose, nine, and the greatest number of hypodermoclyses seventy. All of the infants who survived were given transfusions, as were twenty-one of those who died. The greatest number of transfusions given to a child who survived was nine, and the greatest number given to one who died, fifteen.

Other treatments were given as indicated by the condition of the infant, but none of the other therapeutic agents, such as gentian violet, bacteriophage and erysipelas serum, were used in a large enough number of cases for conclusions as to their efficacy to be drawn.

Prognosis.—Of the thirty-nine infants who had septicemia, thirty-four died. In group I (streptococcus septicemia), consisting of fifteen infants, all died. In group II (staphylococcus septicemia), consisting of eleven infants, three were discharged as well and eight died. In group III (B. coli septicemia), consisting of ten infants, two were discharged as well and eight died. The two infants in group IV (pneumococcus septicemia) and the one infant in group V (B. pyocyaneus and staphylococcus septicemia) died.

The duration of the illness in the fatal cases was, as a rule, short. Fifteen of the thirty-four infants who died succumbed before the end of the first week of illness.

Five of the thirty-nine infants with septicemia survived, three from the staphylococcus group and two from the B. coli group. Of the three with staphylococcus septicemia, one is 5½ years old at the time of this report and is perfectly well; the second was discharged at 1 month of age and is reported to be well at 2 years; the third is 2 years old, but is pale and underweight and has a spastic, right-sided hemiparesis. Of the two with B. coli septicemia, one, now 6½ years old, has evidences of injury to the basal ganglia with severe general motor dysfunction and athetosis; the other, although afebrile and gaining weight, still shows pus cells in the urine at 8 months of age. The possibility of a congenital developmental anomaly of the urinary tract with chronic infection must be considered in the last case.

Postmortem Observations.—Twenty of the thirty-four infants who died were examined post mortem. The diagnoses made post mortem are recorded in the case histories at the end of the paper. Many different lesions were found, the commonest in order of frequency being hemorrhage (ten times), abscesses (nine times), pneumonia (six times) and meningitis, peritonitis and omphalitis (each five times). At postmortem examination, meningitis, peritonitis and omphalitis were each found three times when unsuspected clinically.

A few unusual observations were made at the postmortem examinations, which may be noted as of special interest.

Changes in the liver were found in three cases with marked jaundice (one of staphylococcus, one of B. coli and one of pyocyaneus septicemia). In one case the liver showed chronic hepatitis, in another diffuse fibrosis and in the third central necrosis. In one of these cases with changes in the liver yellow staining of the basal nuclei of the brain was present.[14] The finding of an infection of the blood stream in these cases is of great interest, since the condition is ordinarily diagnosed clinically as icterus gravis. Though a considerable number of similar cases have been reported in the literature blood cultures have rarely been made.

In three cases gastric ulcers were found; in two the ulcers were single and perforated,[15] in the third case there were multiple small ulcers.[16] In the latter case staphylococci were demonstrated in the tissues around the ulcer in stained sections. Omphalitis was present with thrombi in the vessels of the cord, and sections stained for organisms showed cocci in the thrombi. There were also multiple abscesses in the lungs.

SUMMARY

Thirty-nine cases of septicemia in new-born infants occurring in a period of five years in the New Haven Hospital are reported. The final diagnosis, based on the growth of organisms from the blood, was usually corroborated by clinical, and, in many cases, by postmortem examination. The commonest organisms found were the streptococcus, the staphylococcus and B. coli.

Clinically septicemia due to the streptococcus seems to differ from other types of septicemia by the absence of jaundice and bleeding, by the less frequent enlargement of the spleen and by the more frequent appearance of cutaneous infections, omphalitis, peritonitis and meningitis. Streptococcus septicemia invariably had a fatal outcome.

In the cases of septicemia caused by the staphylococcus or by B. coli, on the other hand, jaundice was a common symptom, occurring in more than one half of the cases in both groups. Bleeding took place in about one half of the cases in the staphylococcus group and in about one third of the cases in the B. coli group. The spleen was frequently enlarged (one half or more of the cases) in both groups. Anemia, however, was less common in staphylococcus septicemia than in that caused by the streptococcus and B. coli. Infection of the urinary tract was found only in cases of B. coli septicemia. Staphylococcus or B. coli septicemia was not invariably fatal.

14. This case is being reported by Drs. H. Zimmerman and H. Yannet.
15. These cases are being reported by Drs. E. C. Dunham and R. Goldstein.
16. This case is being reported by Drs. E. C. Dunham and M. T. Shelton.

CONCLUSION

Septicemia, in spite of the general impression to the contrary, is an important and relatively frequent cause of morbidity and mortality in the new-born. Blood cultures should always be taken when a new-born infant becomes ill and the diagnosis is obscure. If the cause of the illness is determined early and transfusions of blood as well as other treatment are given, a number of these infants may recover.

ABSTRACTS OF CASE HISTORIES

GROUP I.—*Case* 1.—J., a boy, was admitted to the hospital at the age of 2 days because of fever. The mother had been admitted eight days before delivery with erysipelas of the face and neck; her temperature was 101 F.; the Wassermann test (blood) was negative. Three blood cultures were negative, but a fourth, made three weeks post partum, showed hemolytic streptococci. A vaginal culture showed hemolytic streptococci. Birth was spontaneous after a precipitate labor. The infant weighed 3,190 Gm.; the temperature was 35.8 C. (96.6 F.); no abnormalities were noted. Two days later fever and erysipelas on the face developed. The child was given erysipelas serum but died shortly thereafter. A postmortem blood culture showed hemolytic streptococci. The diagnosis was erysipelas and streptococcus septicemia. Autopsy was not performed.

Case 2.—B., a boy, was admitted to the hospital at birth because of cyanosis. The mother was admitted the day before delivery with a temperature of 102.8 F. and erysipelas of the face and neck. A culture of her blood made the day after delivery showed hemolytic streptococci. Birth was precipitate after a short labor. The infant was small, premature and very cyanotic. The respirations became weak, and erysipelas developed around the umbilicus and on the thighs. Death occurred at the age of 5 hours. A postmortem blood culture showed hemolytic streptococci. The diagnosis was prematurity, erysipelas and streptococcus septicemia. Autopsy was not performed.

Case 3.—B., a boy, was brought to the hospital at the age of 15 days for postmortem examination. The mother was admitted to a hospital for delivery. The hospital record showed that the membranes ruptured spontaneously, and delivery occurred twenty minutes later. No vaginal examinations were made. There was a deep second degree tear. On the day after delivery the temperature rose and continued elevated. On the seventh day post partum a blood culture was positive for hemolytic streptococci. The infant at the age of 10 days had pustules on the face and erythema of the cheek. He died on the fifteenth day. A blood culture (postmortem) showed hemolytic streptococci. At autopsy the primary diagnosis was omphalitis; erythema and maceration of the eye, cheek and neck; necrotizing pharyngitis, and laryngitis. The subsidiary diagnosis was mastitis.

Case 4.—R. T., a girl, was admitted to the hospital at the age of 23 days with an abscess of the breast. The mother was well; she had had a spontaneous delivery at term. The infant weighed 8 pounds and 11¼ ounces (3,947.6 Gm.). She was breast fed. At the age of 7 days an abscess of the breast developed, and on the nineteenth day erysipelas. On examination the infant was very ill, with a temperature of 39.8 C. (103.8 F.); the spleen was palpable two fingerbreadths below the costal margin; there was erysipelas on the neck, chest, back and extremities. The white blood cells numbered 7,900. The Wassermann test (blood) was negative. Cultures of the spinal fluid and blood, as well as a culture from the

abscess of the breast, showed hemolytic streptococci. The infant was given an immediate transfusion of blood and a hypodermoclysis, but died soon afterward. The diagnosis was erysipelas, meningitis and hemolytic streptococcus septicemia. At autopsy the primary diagnosis was abscess of the breast (right); desquamation of the skin (clinically, erysipelas); congestion of the cerebral vessels, and purulent meningitis (clinically, streptococcus meningitis). The subsidiary diagnosis was patent urachus; patent umbilical arteries, and patent foramen ovale.

Case 5.—R. R., a boy, was admitted to the hospital at birth because of fever. The mother had had a fall two weeks before delivery, following which there was bleeding twice. Delivery was normal and spontaneous. The infant weighed 2,570 Gm. The Wassermann test (blood) was negative. A large abdominal defect was present. The temperature was subnormal for the first week and normal during the second and third weeks. On the twenty-second day bilateral otitis media was found. Two days later the temperature rose and continued to be high until death occurred on the twenty-fifth day. Cultures of the blood and spinal fluid (postmortem) showed hemolytic streptococci. The diagnosis was congenital defect of the abdominal wall, meningitis and hemolytic streptococcus septicemia. At autopsy the primary diagnosis was congenital umbilical hernia, with herniation of the liver, and edema of the scrotum. The subsidiary diagnosis was stenosis of the ureters, with hydro-ureter (bilateral).

Case 6.—T. C., a boy, was admitted to the hospital at the age of 2 weeks because of a cutaneous eruption. The mother was well; she had had a normal, spontaneous delivery at term. The infant weighed 3,730 Gm. He was breast fed. At the age of 2 weeks an eruption developed on the skin which spread rapidly. Examination gave negative results except for impetiginous lesions and purulent discharge from the umbilicus. These lesions healed, but twelve days later the temperature suddenly rose to 39 C. (102.2 F.). New cutaneous lesions appeared which proved to be those of erysipelas. Two blood cultures at this time showed hemolytic streptococci. The Kahn test (blood) was negative. Signs of pericarditis and peritonitis developed, and death occurred on the following day. The diagnosis was erysipelas and hemolytic streptococcus septicemia. Autopsy was not performed.

Case 7.—R. L., a boy, was admitted to the hospital at the age of 7 days because of a cutaneous eruption, irritability and fever. The mother was well. Delivery had been difficult but spontaneous. The infant weighed 8 pounds (3,628 Gm.). Breast and complementary feeding was given. On the day before admission erysipelas developed. Examination gave negative results except for erysipelas and a crust on the stump of the umbilicus. The white blood cells numbered 6,800, with 79 per cent polymorphonuclears. A blood culture and pus from the umbilicus showed hemolytic streptococci. In spite of hypodermoclysis, two blood transfusions and the administration of erysipelas streptococcus antitoxin, the lesions spread, and the child died two days after admission. The diagnosis was erysipelas, peritonitis and streptococcus septicemia. At autopsy the primary diagnosis was necrotizing omphalitis; pericystitis and periureteritis; subcutaneous lymphangitis; general peritonitis, and congestion of the viscera. The subsidiary diagnosis was partial double ureter (bilateral) and hydro-ureter (bilateral).

Case 8.—R. W., a boy, was admitted to the hospital at the age of 1 month because of drowsiness, refusal of food and convulsions. The mother was well. The infant had been delivered by cesarean section. He weighed 10 pounds and 6 ounces (4,706 Gm.). Breast and complementary feeding was given. Convulsions began on the sixth day of life and lasted for three days. The cord was said to be

infected, and irregular fever was present for about two weeks. On examination the infant was poorly nourished and pale; the liver was enlarged from 3 to 4 cm.; the spleen was enlarged 2 cm., and the temperature was 39 C. (102.2 F.). Cultures of the spinal fluid and blood showed hemolytic streptococci. The diagnosis was septicemia and meningitis (Streptococcus hemolyticus). Autopsy was not performed.

Case 9.—P. D., a boy, was admitted to the hospital at the age of 4 weeks because of erysipelas. The illness began four days before admission with irritability and vomiting. On the next day fever and redness of the left eyelid developed; the redness then spread to the face and scalp. On examination the infant was very ill; breathing was rapid and irregular; there were lesions of erysipelas on the face, and the temperature was 40 C. (104 F.). A blood culture showed hemolytic streptococci. The white blood cells numbered 6,100, with 82 per cent polymorphonuclears. The Kahn test (blood) was negative. The infant received hypodermoclyses and two transfusions of blood, but the lesions spread and signs of peritonitis developed. Death occurred two days after admission. The diagnosis was erysipelas and hemolytic streptococcus septicemia. Autopsy was not performed.

Case 10.—J. B., a girl, was admitted to the hospital at the age of 12 days because of refusal of feedings. The mother was well. She had had a normal labor and delivery. The infant weighed 7 pounds and 14 ounces (3,572.04 Gm.). Feeding was artificial. There had been frequent stools since birth; the child had vomited twice and was brought in because of refusal to take food. On examination the infant was dehydrated and thin; the breathing was slow and deep, and there were a pustule on the shoulder and excoriation of the buttocks. The temperature was 35.2 C. (95.4 F.). The weight was 2,420 Gm. White blood cells numbered 26,500 with 66 per cent polymorphonuclears. The Wassermann test (blood) was negative. One blood culture was negative, and two showed hemolytic streptococci. Hypodermoclyses and intravenous injections of dextrose were given. Otitis media developed and an abscess on the cheek which was incised. Cultures from the pus showed hemolytic streptococci. Cellulitis of the neck then developed, which went on to necrosis. The infant received two blood transfusions but died five days after admission. The diagnosis was suppurative otitis media, abscess of the cheek and hemolytic streptococcus septicemia. At autopsy the primary diagnosis was necrosis of the cheek (left) and pharynx; edema of the larynx; otitis media (bilateral), and mastoiditis (right). The subsidiary diagnosis was supernumerary toe and hemorrhage into the pleura and peritoneum. Culture of the heart's blood showed hemolytic streptococci.

Case 11.—M. S., a boy, was admitted to the hospital at the age of 6 weeks because of a cold of two weeks' duration. The mother was well. Delivery had been spontaneous at term. The infant's weight was 7¾ pounds (3,515.34 Gm.). He was breast fed for three weeks. The onset of illness was indefinite, but a convulsion occurred four days before admission. On examination the infant was moderately dehydrated and hypertonic. There were an inguinal hernia, thrush and purulent otitis media. The temperature was 38.2 C. (104.8 F.). A blood culture showed hemolytic streptococci. Saline solution was given subcutaneously and intraperitoneally. A lumbar puncture yielded bloody fluid. Death occurred two days after admission. The diagnosis was malnutrition with atrophy; thrush; bilateral purulent otitis media, and hemolytic streptococcus septicemia. Autopsy was not performed.

Case 12.—C. F., a boy, was admitted to the hospital at the age of 25 days because of omphalitis. The mother was well. Delivery had been spontaneous at

term. The infant's birth weight was not known. He was breast fed. The cord separated on the eighth day, but a few days later discharge began and redness appeared, which involved the penis and scrotum also. On examination the infant was thin; there were an infected ulcerated area on the abdomen and penis and induration of the scrotum and testicles; the temperature was 36.8 C. (98.2 F.). The white blood cells numbered 46,000, with 70 per cent polymorphonuclears. The Wassermann test (blood) was negative. A blood culture showed Streptococcus hemolyticus. A transfusion was given. Signs of pneumonia developed two days after admission, and the infant died on that day. The diagnosis was ulcer of the umbilicus, hypospadius, acute nonsuppurative orchitis and hemolytic streptococcus septicemia. Autopsy was not performed.

Case 13.—J. B. W., a boy, was admitted to the hospital at the age of 33 days because of erysipelas. The mother died from pneumonia about six days post partum. The infant's birth weight was 8 pounds (3,629 Gm.). The type of delivery and the kind of feeding given are not known. Diarrhea, vomiting and infection of the upper respiratory tract developed soon after birth. At the age of 3 days a red area appeared on the nose. On examination the infant was small, thin and dehydrated; there were a severe, purulent nasal discharge and erysipelas; the spleen was palpable, and otitis media was present. The temperature was 38.6 C. (101.4 F.). The white blood cells numbered 26,500, with 57 per cent polymorphonuclears. A blood culture showed hemolytic streptococci and staphylococci. Hypodermoclyses, blood transfusions and intravenous injections of dextrose were given. The lesions spread to the neck and the abdomen. The child died two days after admission. Postmortem blood culture showed hemolytic streptococci. The diagnosis was erysipelas and hemolytic streptococcus septicemia. Autopsy was not performed.

Case 14.—A. G., a girl, was admitted to the hospital at the age of 40 days because of fever. There had been a normal spontaneous delivery at home. "Milk leg" developed in the mother two or three days after delivery. The infant's birth weight was about 10½ pounds (4,763 Gm.). She was breast fed for two weeks and then put on formula. At 15 days of age, an infection of the upper respiratory tract with fever developed. Later osteomyelitis of the right knee was diagnosed; on the thirty-second day operation was performed; two days later cutaneous lesions appeared. On admission the infant was vigorous and well nourished, with extensive, erysipelas-like lesions of the trunk and the right leg and foot. The temperature was 39.2 C. (102.6 F.). The white blood cells numbered 12,900, with 80 per cent polymorphonuclears. The Kahn test (blood) was negative. Culture of the blood and of pus from the incision in the leg showed hemolytic staphylococci. Five transfusions of blood were given. The infant gradually became weaker as the erysipelas spread and died six days after admission. A postmortem blood culture showed hemolytic streptococci, as did fluid aspirated from the chest. The diagnosis was hemolytic streptococcus septicemia, cellulitis of the leg and erysipelas (?). Autopsy was not performed.

Case 15.—D. N., a boy, was admitted to the hospital at the age of 4 days because of fever and loss of weight. The mother had a postpartum hemorrhage. Birth was spontaneous at term. The membranes ruptured twenty hours before delivery. The infant's birth weight was 3,755 Gm. At the age of 4 days a high temperature developed, which continued. On examination the infant was somewhat spastic; there were blue spots on the buttocks, ankle and umbilicus; the abdomen was tense, and there was otitis media. The temperature was 40.4 C. (104.8 F.). The white blood cells numbered 4,450, with 23 per cent polymorphonuclears. Cultures of the spinal fluid and blood showed nonhemolytic streptococci. A blood smear showed

gram-positive streptococci. The infant became rapidly worse and died on the eighth day of life. The diagnosis was infection of the umbilical cord, acute otitis media, streptococcus septicemia, meningitis and peritonitis. At autopsy the primary diagnosis was acute purulent omphalitis; acute purulent peritonitis; pleurisy; meningitis; abscess of the brain; acute splenic tumor, and cloudy swelling of the viscera. There was no subsidiary diagnosis.

GROUP II.—*Case* 16.—R. T., a boy, was admitted to the hospital at birth because of jaundice and enlarged spleen. The mother was well. There had been a normal spontaneous delivery at eight months. The infant's birth weight was 1,830 Gm. On examination the child was small and jaundiced; the spleen was enlarged, and a few petechiae were scattered over the trunk. The temperature was normal. Hemoglobin was 110 per cent; red blood cells numbered 5,900,000, and white blood cells, 12,300, with 39 per cent polymorphonuclears and 46 per cent lymphocytes. The urine was normal. A blood culture on the third day showed staphylococci. The infant received five transfusions of blood and six intravenous injections of dextrose. He was discharged at 64 days of age in good condition after ten negative blood cultures were obtained. The diagnosis was staphylococcus septicemia.

Case 17.—G. W., a boy, was admitted to the hospital at the age of 13 days because of jaundice and fever. The mother had had two previous pregnancies. The first child had hemorrhagic disease of the new-born. The second child was prematurely born at six months and died one-half hour after birth. During the third pregnancy the mother had a severe secondary anemia and hydramnios. Labor was induced by artificial rupture of the membranes; delivery was spontaneous. The infant was feeble and slightly cyanotic. The birth weight was 8 pounds and 2 ounces (3,685.44 Gm.). On the eighth day he collapsed and was found to have fever; on the thirteenth day diarrhea and distention developed, and he had jaundice and an enlarged liver and spleen. The stools were light-colored, and the urine dark. Hemoglobin was 135 per cent; red blood cells numbered 5,665,000, and white blood cells 10,600, with 38 per cent polymorphonuclears and 61 per cent lymphocytes. The course was characterized by increasing jaundice, daily fever and severe diarrhea. Transfusions of blood and hypodermoclyses were given. Frequent blood cultures were made, three of which were positive for staphylococci. A blood culture on the twenty-seventh day of life showed many deep colonies of a hemolytic staphylococcus. Because of increasing jaundice and acholic stools the patient was subjected to an exploratory operation; cholecystotomy was done, and after a stormy course bile appeared in the stools, the jaundice cleared, and the infant made a complete recovery. At the time of this report he is 5½ years old and weighs 55 pounds (24.9 Gm.). The diagnosis was staphylococcus septicemia.

Case 18.—D. G., a boy, was admitted to the hospital at the age of 17 days because of jaundice and hematuria. He was born spontaneously at term; labor was prolonged after premature rupture of the membranes. Jaundice, which appeared about the third day, became increasingly intense; the stools were yellow, and hematuria occurred on the day of admission. On examination the infant was emaciated and deeply jaundiced; the temperature was subnormal; the liver and spleen were enlarged; the stools were light-colored, and the urine was bright red. Hemoglobin was 160 per cent; red blood cells numbered 6,328,000, and white blood cells, 24,000, with 44 per cent polymorphonuclears and 55 per cent lymphocytes; the platelets were normal. The Wassermann test (blood) was negative. Four blood cultures were made, three of which showed staphylococci. The course was characterized by failure to gain weight, variable jaundice and colorless stools alternating with bile-colored ones. Frequent transfusions of blood and hypodermoclyses were

given. An exploratory laparotomy was done. In spite of a normal gallbladder and extrahepatic ducts, cholecystotomy and cholecystogastrostomy were done. Otitis media developed, and the infant died. At autopsy the primary diagnosis was: (*A*) chronic hepatitis, malnutrition, dehydration, old operations and choledochotomy; (*B*) cholecystogastrostomy for establishment of bile drainage and adhesions about the operative site. The subsidiary diagnosis was patent ductus arteriosus.

Case 19.—E. T., a boy, was admitted to the hospital at the age of 6 weeks because of multiple abscesses. The mother was well; she had had no other pregnancies. The infant was delivered by cesarean section. The birth weight was 9 pounds and 12 ounces (4,422.53 Gm.). Breast feeding with complementary feeding was used. The child was circumcised on the eighth day by a rabbi. The cord separated on the twenty-seventh day, and the stump was red. Inflammation of the penis and multiple abscesses developed. On examination the infant was deeply jaundiced, with draining abscesses which had been incised. The spleen was very large; the umbilicus and penis were healed, and there was slight inguinal adenitis. The temperature was 39.2 C. (102.6 F.). Red blood cells numbered 2,816,000; hemoglobin was 60 per cent, and white blood cells numbered 5,200, with 48 per cent polymorphonuclears. A blood culture showed Staphylococcus aureus. A transfusion of blood and two intravenous injections of gentian violet were given. The infant died on the day of admission. The diagnosis was Staphylococcus aureus septicemia. Autopsy was not performed.

Case 20.—A. S., a boy, was admitted to the hospital on the first day of life because of prematurity. The mother had grip one week before delivery. Delivery was spontaneous after premature rupture of the membranes (two days). The infant's cry was delayed; cyanosis was present, which became more marked. Examination gave negative results, except for a feeble cry; the temperature was 38.2 C. (100.8 F.); the weight was 1,730 Gm.; the Kahn test (blood) was negative; white blood cells numbered 25,200, with 37 per cent polymorphonuclears, and two blood cultures were negative. The infant had repeated attacks of severe cyanosis. Several hypodermoclyses, intravenous injections of dextrose and a transfusion of blood were given. A smear from the eyes showed gram-negative cocci. On the second day marked jaundice and distention appeared. A profuse hemorrhage occurred from the mouth and nose, and the infant died on the following day. A postmortem blood culture showed staphylococci; a culture of the peritoneal fluid showed staphylococci and nonhemolytic streptococci. The clinical diagnosis was septicemia (staphylococcus and hemolytic streptococcus), prematurity, gonorrheal ophthalmia and hemorrhage, subcutaneous and gastric. At autopsy the primary diagnosis was acute omphalitis; thrombi in the gastric and pulmonary vessels; multiple gastric ulcers; focal pneumonia and partial pulmonary atelectasis, and prematurity. The subsidiary diagnosis was hematoma of the scalp and acute (gonorrheal) conjunctivitis (bilateral).

Case 21.—L., a boy, was admitted to the hospital soon after birth because of dehydration, pallor, cyanosis and fever. The mother was well. There had been a mid-forceps delivery after a labor of twenty-four hours. The membranes were ruptured artificially seven hours before delivery. At birth the infant was somewhat dehydrated. The following day this became more marked. On examination he was pale; the temperature was 39 C. (102.2 F.); the tip of the spleen was palpable, and there were slight jaundice and generalized desquamation. The Wassermann test (blood) was negative. Blood cultures on the second, fourth, sixth, ninth and fifteenth days showed staphylococci. One transfusion of blood was given. The infant was discharged well at the age of 25 days, after three negative blood cultures

were obtained. He is well at the time of this report, at the age of 2 years. The diagnosis was staphylococcus septicemia.

Case 22.—B., a girl, was admitted to the hospital at the age of 2 days because of fever, vomiting and a cutaneous eruption. The mother was well; the Wassermann test (blood) was negative. The infant, the eighth child, was delivered spontaneously, with a birth weight of 3,810 Gm. She was breast fed. She appeared normal at birth, but on the following day the temperature was slightly elevated, on the third day of life the stools contained a small amount of blood, and on the fourth day areas of erythema with desquamation appeared on the face. Examination gave negative results except for lesions of the skin. The temperature was 38.6 C. (101.4 F.). The white blood cells numbered 25,600, with 78 per cent polymorphonuclears; the clotting time was five and one-fourth minutes. A blood culture showed staphylococci. The infant was given hypodermoclyses and intravenous injections of dextrose. On the following day she vomited bloody material; a transfusion of blood was given, but she died at the age of 4 days. The spleen became palpable 1 cm. below the costal margin. The diagnosis was exfoliative dermatitis and staphylococcus septicemia. At autopsy the diagnosis was exfoliative dermatitis (staphylococci were grown from the heart's blood, lungs, liver, kidney and spleen); subcutaneous hemorrhages; hemorrhagic pneumonia (bilateral); enteritis, and meningitis.

Case 23.—R. J., a boy, was admitted to the hospital at the age of 1 month because of an abscess on the back, labored breathing and vomiting. Delivery was said to be normal. The infant weighed 9¾ pounds (4,422.53 Gm.), and was considered well until 3 weeks old when an "infected insect bite on the cheek" developed, followed by an abscess on the back. Both of these were incised. Fever was present. On the day before admission the infant vomited, and his condition seemed worse. On examination he was cyanotic and *in extremis.* There were an incision on the back with pus draining and an abscess on the left hand; the liver was greatly enlarged, and the spleen palpable. The patient died about twenty minutes after arrival at the hospital. Postmortem cultures of the blood and spinal fluid showed staphylococci. The diagnosis was staphylococcus septicemia, bronchopneumonia and abscesses on the hand and back. At autopsy the diagnosis was abscess in the tissues of the back (right) and generalized embolic abscesses.

Case 24.—J. M., a boy, was admitted to the hospital at the age of 13 days because of fever. The mother was well; the Wassermann test (blood) was negative. Delivery was normal and spontaneous at term. The membranes ruptured about thirty-six hours before delivery. The placenta showed no evidence of infection. The birth weight was 3,720 Gm. The child was breast fed. At the age of 11 days a temperature of 39 C. (102.2 F.) developed, and the patient showed a dusky cyanosis and a slightly red throat. A blood culture showed Staphylococcus aureus. On the following day the arm appeared weak, and the fever continued. The white blood cells numbered 19,500, with 66 per cent polymorphonuclears and 33 per cent lymphocytes. The infant received two transfusions of blood. The left shoulder then became swollen, but roentgenograms were negative. Abscesses developed on the toe, and in the ankle and hip. The baby died on the thirtieth day of life. The diagnosis was staphylococcus septicemia and osteomyelitis. At autopsy the diagnosis was otitis media (bilateral) (clinically, septicemia); osteomyelitis of the right tibia, left humerus, first right metatarsal and right humerus; necrotizing peritonitis, pericarditis, focal pneumonia and pleuritis; multiple subpleural and subendocardial hemorrhages; multiple subcutaneous abscesses, and purulent cerebrospinal meningitis.

Case 25.—R. Z., a girl, was admitted to the hospital at birth because of prematurity. The mother had toxemia. The infant was delivered by cesarean section; the birth weight was 1,612 Gm. Feeding was with breast milk. On the seventeenth day fever developed. Examination gave negative results except for small size, pallor and cyanosis. The temperature was 35.2 C. (95.4 F.); the white blood cells numbered 20,360. The bleeding and coagulation times were normal. The Wassermann test (blood) was negative. A blood culture showed staphylococci. Hypodermoclyses, intravenous injections of dextrose and transfusions of blood were given. On the twentieth day the infant vomited dark blood, and died about twenty-four hours later. The diagnosis was prematurity and staphylococcus septicemia. Autopsy was not performed.

Case 26.—H. A., a boy, was admitted to the hospital at the age of 15 days because of vomiting. The mother, said to be in poor health, had been delivered by low forceps at term. The Kahn test of the mother's blood was negative. The infant's birth weight was 4,170 Gm. He was breast fed. On the fifth day one or two impetiginous lesions developed which did not spread. On the fourteenth day vomiting began, which continued to the time of admission. Examination gave negative results, except for malnutrition. The spleen was palpable. The temperature was 37.6 C. (99.6 F.); the white blood cells numbered 13,250, with 39 per cent polymorphonuclears and 60 per cent lymphocytes. The infant received one hypodermoclysis. A blood culture showed staphylococci. The infant died four days after admission. The diagnosis was malnutrition and staphylococcus septicemia. Autopsy was not performed.

GROUP III.—*Case* 27.—S. H., a boy, was admitted to the hospital at birth because of jaundice. The mother had a normal pregnancy, but thrombophlebitis of the saphenous vein developed post partum. Delivery was spontaneous. At birth the infant was jaundiced. On the ninth day of life the spleen was enlarged, and on the twelfth day he bled from a scratch on the cheek and ecchymotic areas appeared on the skin. The liver became enlarged. The stools varied from pale to dark yellow. Hemoglobin was 25 per cent; red blood cells numbered 2,562,000, and white blood cells, 15,280, with 62 per cent polymorphonuclears and 38 per cent lymphocytes. During the first three weeks of life the illness was characterized by fever, deep jaundice and a tendency to bleed. Osteomyelitis of the upper end of the right humerus developed. Frequent blood transfusions were given. Three blood cultures showed Bacillus coli. After the first month the temperature gradually fell to normal; the jaundice became less intense, and the infant was discharged after sixty-five days in the hospital. At the time of this report he is 6½ years old and is mentally and physically retarded. He has the type of athetosis associated with a lesion in the basal ganglions of the brain. The diagnosis was B. coli septicemia and osteomyelitis of the humerus.

Case 28.—J. R., a boy, was admitted to the hospital at the age of 28 days because of fever. There had been a normal spontaneous delivery. The infant had not done well since discharge from the hospital where he was born; he vomited occasionally, and his abdomen had become progressively enlarged. A pustule developed on the left leg eight days before admission. The night before admission he was found to have a temperature of 101.2 F. On examination he was malnourished and deeply jaundiced and had a subnormal temperature; the abdomen was greatly distended. Hemoglobin was 90 per cent; the red blood cells numbered 4,000,000, and the white blood cells, 44,000, with 55 per cent polymorphonuclears and 35 per cent lymphocytes. A blood culture showed B. coli. The patient was given a trans-

fusion of blood, but died shortly afterward. At autopsy the primary diagnosis was diffuse fibrosis of the liver; jaundice; ascites; splenomegaly, and pulmonary hemorrhage.

Case 29.—N. S., a boy, was admitted to the hospital on the fourth day of life because of fever and vomiting. The mother had toxemia; the infant was delivered by cesarean section at term. He weighed 4,166 Gm. Feeding was artificial. On the fourth day, although previously well, the infant vomited and signs of peritonitis developed rapidly. The white blood cells numbered 4,000, with 38 per cent polymorphonuclears. The Wassermann test (blood) was negative. A blood culture showed B. coli. At operation perforation of the stomach was found. Repair was attempted, but the infant died on the twenty-first day of life. The diagnosis was perforation of the stomach and B. coli septicemia. At autopsy the primary diagnosis was perforation of the stomach; localized peritoneal abscess; subdiaphragmatic abscess (left); partial obstruction of the sigmoid colon; fecal fistula, and focal pneumonia. The subsidiary diagnosis was recent laparotomy for drainage and suture of the stomach.

Case 30.—F. M., a girl, was admitted to the hospital at the age of 62 hours because of bleeding from the nose and hematuria. The mother was well. Delivery was normal. The infant was born prematurely. The birth weight was not reported. The type of feeding is not known. On the day before the patient's admission the mother noticed bleeding from the nose and jaundice. The baby had several convulsions before admission. On examination she was jaundiced; there were a small amount of dried blood in the right nostril and a large ecchymotic area on the hard palate; there was slight bleeding from the rectum. The white blood cells numbered 16,000, with 47 per cent polymorphonuclears. A blood culture showed B. coli. The infant vomited coffee-ground material and passed a black stool. She was given intramuscular and intravenous injections of blood. She had several convulsive seizures, became very cyanotic, and died less than twenty-four hours after admission. The diagnosis was B. coli septicemia and hemorrhage from the gastro-intestinal tract. Autopsy was not performed.

Case 31.—G. G., a boy, was admitted to the hospital at birth because of an enlarged spleen and jaundice. The mother was well. Delivery was normal and spontaneous. The mother's first child had died at the age of 3 weeks with fever and hemorrhages. The second child had severe anemia at the age of 2 weeks, but recovered following two transfusions. The mother bruised easily. The infant was observed with special care because of the family history of bleeding. He was given blood immediately after birth, and then adult serum for several days. The jaundice that appeared shortly after birth deepened, and marked anemia developed. The bleeding time was one minute and twenty seconds, and the coagulation time, four and one-half minutes on the day of birth. The red blood cells numbered 4,100,000; hemoglobin was 90 per cent, and the white blood cells 16,600, with 45 per cent polymorphonuclears; the platelet count was 340,000, and reticulated red blood cells were 13 per cent. The fragility test was normal. During the second week fever was present. At the age of 15 days, the right kidney was found to be enlarged; a blood culture showed B. coli. The urine, on repeated examinations, showed numerous pus cells in clumps; gram-negative bacilli were demonstrated in smears; colon bacilli were grown in two cultures made from the urine. Transfusions of blood were given, but the infant died at the age of 25 days. The diagnosis was B. coli septicemia and acute purulent pyelonephritis. At autopsy the primary diagnosis was acute suppurative nephritis with multiple abscesses (bilateral) (clinically, B. coli septicemia); serofibrinous peritonitis; focal pneumonia (bilateral), and jaundice. The subsidiary diagnosis was suprarenal rest in the testes.

Case 32.—G., a boy, was admitted to the hospital at birth because of prematurity. The mother was eclamptic; labor was induced prematurely, and delivery was precipitate. The infant weighed 2,140 Gm. He cried only after prolonged stimulation. A few hours after birth he vomited a small amount of fresh blood. Examination showed a small baby, with shallow breathing and a feeble cry. The temperature was not taken. A blood culture showed B. coli. A nasal swab showed an almost pure culture of B. coli. The coagulation time was six minutes. Bleeding from the mouth continued. The child was given a transfusion of blood. Signs of fluid in the chest developed, paracentesis was done, and bloody fluid was withdrawn from which a pure culture of B. coli was grown. The infant died twenty hours after birth. The diagnosis was hemorrhagic disease of the new-born, prematurity and B. coli septicemia. At autopsy the primary diagnosis was undetermined; there were multiple hemorrhages into the viscera, brain and meninges. A blood culture showed B. coli.

Case 33.—B., a boy, was admitted to the hospital at birth because of prematurity and vomiting. Delivery had been premature and spontaneous. The puerperium was febrile. The infant weighed 1,960 Gm. Feeding was artificial. Vomiting of bile-stained fluid began almost immediately after the first feedings. Attacks of cyanosis and abdominal distention developed. Examination showed a vigorous infant with bilateral cleft palate and harelip. The Wassermann test (blood) was negative. The temperature was 35.6 C. (96 F.). Roentgenograms of the abdomen showed distention of the stomach and intestines. Hypodermoclyses were given. The infant died at the age of 2 days. A postmortem blood culture showed B. coli, as did peritoneal fluid aspirated post mortem. The diagnosis was prematurity, cleft palate, harelip and B. coli septicemia. At autopsy the primary diagnosis was hemorrhage in the wall of the stomach (cardia), gangrene and perforation of the stomach and diffuse peritonitis. The subsidiary diagnosis was prematurity and cleft palate (bilateral).

Case 34.—L., a girl, was admitted to the hospital one and one-half hours after birth because of prematurity. The mother was well. The infant was born precipitously before the arrival of a physician. The birth weight was 1,670 Gm. Artificial feeding was given. Examination showed a small baby with periodic attacks of pallor and cyanosis; there were crepitant râles over the back; the spleen was not palpable. The temperature was 35 C. (95 F.). The white blood cells numbered 8,000, with 62 per cent polymorphonuclears. The temperature continued subnormal; feeding was difficult. The child became severely jaundiced, and diarrhea developed. She received frequent hypodermoclyses. She died ten days after admission. A postmortem blood culture showed B. coli. The diagnosis was icterus gravis, diarrhea and dehydration and B. coli septicemia. At autopsy the diagnosis was suppurative omphalitis, jaundice of the nuclear masses of the brain and prematurity.

Case 35.—D. H., a girl, was admitted to the hospital at the age of 16 days because of poor color and labored breathing. The mother was well. There had been a normal spontaneous delivery. The infant was thought to be well until the day before admission when she seemed a little irritable, her color was poor, breathing was labored, and she refused her feeding. On the way to the hospital the infant was severely burned by a hot water bottle. On examination the temperature was 38.8 C. (101.8 F.). The infant was in collapse. The breathing was rapid and shallow, the extremities were cyanotic, the anterior fontanel was sunken, the left ear drum was dull, occasional râles were heard in the left axilla, and the spleen was palpable. There was a third degree burn on the right buttock and thigh and both legs. The white blood cells numbered 22,350, with 68 per cent polymorphonuclears and 30 per cent lymphocytes. A blood culture showed B. coli

nine days after admission; the urine showed many white blood cells in clumps. The temperature continued elevated. The infant received dextrose intravenously, numerous hypodermoclyses and transfusions of blood. Rhythmic twitching of the left eyelid, arm and leg developed. Bloody fluid was obtained by lumbar puncture. A roentgenogram of the chest showed bilateral bronchopneumonia. The infant died thirty-six days after admission. The diagnosis was intracranial hemorrhage, third degree burns and B. coli septicemia. At autopsy the primary diagnosis was third degree burns of both feet and the right buttock; abscess on the plantar surface of the right foot; suppurative nephritis; thrombophlebitis of the meningeal vessels; purulent cerebral meningitis, and cerebral abscess.

Case 36.—G. S., a boy, was admitted to the hospital at the age of 16 days because of fever. The mother was well. There had been a forceps delivery at term after a four hour labor. The infant weighed about 8 pounds (3,628 Gm.). He was breast fed. On the tenth day of life fever and cyanosis developed. The next day pus cells were found in the urine. On examination at admission the infant was well nourished; the spleen was slightly enlarged, and the kidneys were palpable, the left larger than the right. Blood culture showed B. coli. The Kahn test (blood) was negative. The white blood cells numbered 13,000, with 65 per cent polymorphonuclears and 24 per cent lymphocytes. The infant was given hypodermoclyses, transfusions of blood and intravenous injections of dextrose. A blood culture made eight days after admission was negative. He was discharged on the seventy-second day of life; the spleen was still enlarged; the kidneys were not palpable, and the urine was loaded with pus cells. There was no fever for two weeks, and the patient gained 950 Gm. He was 6 months old and well at the time of this report. The diagnosis was B. coli septicemia and pyelonephritis.

GROUP IV.—*Case 37.*—P. F., a boy was admitted to the hospital at the age of 1 day because of prematurity. The mother's membranes ruptured six days before delivery. There was a normal, spontaneous birth. The infant weighed about 3 pounds (1,360 Gm.). On examination he was small and cold with shallow respirations. The temperature was subnormal. Frequent cyanotic spells developed and the child died suddenly on the day following admission. A postmortem blood culture showed pneumococci (group IV). The diagnosis was prematurity, atelectasis and pneumococcus septicemia. Autopsy was not performed.

Case 38.—G. P., a girl, was admitted to the hospital at the age of 18 days because of refusal of food and diarrhea. The details of birth are not known. The birth weight was 6 pounds and 6 ounces (2,897.65 Gm.). The infant was considered well until she was 16 days old, when she refused food and diarrhea developed. On examination the infant was moribund, and there were marked rigidity, cyanosis, conjunctivitis and otitis media. The spleen was slightly enlarged. The Wassermann test (blood) was negative. The spinal fluid, pus from the parotid gland and a blood culture showed staphylococci, pneumococci (group IV) and B. coli. Hypodermoclyses, a transfusion of blood and intravenous injections of dextrose were given, but death occurred on the day of admission. The diagnosis was septicemia (pneumococcus [group IV], staphylococcus and B. coli), and abscess of the parotid gland (left). Autopsy was not performed.

GROUP V.—*Case 39.*—J. B., a boy, was admitted to the hospital at the age of 15 days because of loss of weight and diarrhea. The mother was well. There had been a normal delivery after a labor lasting two hours. The infant weighed 6 pounds and 6 ounces (2,897.65 Gm.). He was breast fed for three days. He seemed weak, did not suck well and lost weight. There was a history of bleeding at the age of 1 week. At 10 days vomiting occurred, followed by diarrhea and

jaundice. On examination the infant was emaciated and moderately jaundiced. There was swelling of the left sternoclavicular joint; the spleen was not palpable. The temperature was 38.6 C. (101.4 F.). A roentgenogram of the left clavicle showed osteomyelitis. The white blood cells numbered 53,000, with 85 per cent polymorphonuclears and 15 per cent lymphocytes. The Kahn test (blood) was negative. A blood culture showed B. pyocyaneus and staphylococci. Hypodermoclyses, intravenous injections of dextrose and transfusions of blood were given, but the infant died eleven days after admission. The diagnosis was septicemia (B. pyocyaneus and staphylococcus), prematurity and osteomyelitis of the clavicle (left). At autopsy the diagnosis was *(A)* prematurity and *(B)* acute osteomyelitis (left clavicle), purulent arthritis (left sternoclavicular joint), emaciation, jaundice (clinically, septicemia), and central necrosis of the liver.

EXPERIMENTS ON THE ANTIBACTERIAL PROPERTIES OF PYRIDIUM AND SERENIUM

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The problem of urinary antisepsis is an old one. There has been for years an effort to provide a satisfactory urinary antiseptic for the infectious conditions involving the genito-urinary system. From time to time new preparations are suggested. However, after clinical and experimental studies with these so-called antiseptics, it is conclusive from reported results that an entirely suitable drug has not yet been presented. After a "heyday" of varying length the popularity of each has waned when it has been found to be lacking in one or more of the qualifications for ideal urinary antiseptics suggested by Hinman [1] and later by Davis.[2] The ideal urinary antiseptic should be chemically stable and nontoxic in therapeutic doses. It should be eliminated in high percentage by the kidneys, should exert antiseptic action in high dilution in urines of varying reactions and should, of course, be non-irritating to the genito-urinary tract. Leonard [3] has also added that the antiseptic should be administrable by mouth and should be eliminated in the urine in sufficient concentrations to exert local antiseptic action, at a rate by which continuous antiseptic action can be maintained.

PYRIDIUM

A commercial preparation in common use at the present time, advocated for its chemotherapeutic properties, is pyridium. Study of this compound was prompted by the fact that in the Mayo Clinic satisfactory clinical results had not been obtained with the drug in a group of cases of infections of the upper part of the urinary tract, owing to

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1. Hinman, Frank: Urinary Antisepsis: A Clinical and Bacteriologic Study, J. A. M. A. **65**:1769 (Nov. 20) 1915.

2. Davis, E. G.: Urinary Antisepsis, J. A. M. A. **70**:581 (March 2) 1918.

3. Leonard, Veader: Secretion of Bactericidal Urine and Disinfection of the Urinary Tract, J. A. M. A. **83**:2005 (Dec. 20) 1924.

some of the more common pathogenic organisms, namely, colon bacilli, Staphylococcus aureus and, in a few cases, streptococcus. Pyridium was described by Ostromislensky [4] in 1926 and advocated as a highly efficient bactericidal agent in infections, particularly those of the genito-urinary tract. Gratifying results following the use of pyridium in the treatment of gonorrheal infections of the urethra, prostate gland, seminal vesicles and epididymis have been reported by numerous authors.[5] Also, cystitis and infections of the upper part of the urinary tract, pyelitis and the forms of so-called pyelonephritis, according to many of the same and other writers,[6] are amenable to treatment with pyridium.[7]

Chemically, pyridium is phenylazo-2-6 diamino pyridine monohydrochloride and contains 28 per cent nitrogen. The drug has marked penetrative powers. Meyer [8] has shown that when given intravenously it causes distinct discoloration of the uterine mucosa. Belfield and Rolnick [9] demonstrated that pyridium given intravenously to dogs colored the body of the epididymis and also stained the heads of some of the spermatozoa.

Pyridium is usually administered orally in doses of 0.2 Gm. three times daily, either in tablets or as powder in capsules. The ointment or aqueous solutions have also been used locally to promote epithelization and to stimulate granulation in surgical conditions. Müller [10] said that when pyridium was given by mouth to animals and to adult human beings, there was no toxic effect, but that among children it frequently caused nausea and vomiting. In the experiments reported in this paper no untoward effects were noted following the taking of pyridium by

4. Ostromislensky, I. I.: The Scientific Basis of Chemotherapy, New York, Inter-American Publishing Company, 1926, pt. 1.

5. Deakin, R.: The Efficacy of Pyridium in Gonococcal Urethritis, J. Missouri M. A. **28**:123 (March) 1931. Mason, L. M.: Pyridium Therapy in Genito-Urinary Diseases, Virginia M. Monthly **58**:190 (June) 1931. Pugh, W. C.: Infections of the Urinary Tract, M. J. & Rec. **127**:414 (April 18) 1928; Infections of Urinary Tract: Prostatic Lesions, ibid. **129**:155 (Feb.) 1929. Walther, H. W. E.: Clinical Application of Urinary Antisepsis, South. M. J. **22**:161 (Feb.) 1929. Wolbarst, A. L.: A Study of a New Antiseptic in Urinary Infections, Internat. J. Med. & Surg. **43**:499 (Sept.) 1930.

6. Orlowski: Ueber Pyridium bei Störungen im Urogenitaltakrus, Ztschr. f. Urol. **24**:838, 1930. Stern, R.: Klinische Erfahrungen mit Pyridium einem neuen Harnantisepticum, Klin. Wchnschr. **8**:1358 (July 16) 1929.

7. Pyridium, J. A. M. A. **95**:34 (July 5) 1930.

8. Meyer, J. L.: The Elimination of Dyes by the Uterine Mucosa, J. Lab. & Clin. Med. **14**:936 (June) 1929.

9. Belfield, W. T., and Rolnick, T. C.: Observations on the Physiology and Therapy of the Seminal Ducts, J. A. M. A. **89**:2105 (Dec. 17) 1927.

10. Müller, F.: Erfahrungen mit Pyridium bei septischen Erkrankungen, München. med. Wchnschr. **78**:233 (Feb. 6) 1931.

mouth. The literature is indefinite as to contraindications to the administration of pyridium, but several authors have agreed that it should be withheld in the presence of uremia, severe noninfectious disorders of the kidneys, severe hepatitis when excretion is low and chronic parenchymatous nephritis with a low output of phenolsulphonphthalein. As far as I know, no instance of renal irritation following the administration of pyridium is to be found recorded in the literature. Examination of the urine from a normal adult following the taking of 1 Gm. of the drug during a period of twenty-four hours failed to show any evidence of renal irritation. It is advised that the drug be not used in connection with compounds containing mercury, for it releases the mercury from such compounds.

To determine the amount of pyridium excreted in the urine and the concentration that could be obtained, I took tablets containing 0.1 Gm. Previously I had been examined and pronounced normal. The stained urine was compared colorimetrically with a standard of known concentration. The urinary stream was stained from a light orange to a deep red, or at times almost brown, depending on the amount of drug taken. Pyridium ingested by mouth appeared in the urine in from forty-five minutes to one and a half hours. Considerably greater concentrations were made possible by a restriction of the intake of fluids, and this was done in order to obtain the drug in a concentration from which might be expected the greatest possible antisepsis. No irritation was experienced in voiding urine containing pyridium.

A 1:200 stock solution was made by dissolving pyridium powder in distilled water. The powder was only slightly soluble in cold water, but by boiling for twenty minutes a stable, supersaturated solution could be prepared. Aqueous solutions of the dye were extremely acid. The p_H of the stock solution as determined by the quinhydrone electrode method was 3.73.[11]

One gram of the drug was taken in doses of 0.2 Gm. over a period of twenty-four hours. Three separate specimens were collected in that time, and colorimetric determinations were made on each, and the concentration of the drug for each 100 cc. of urine was calculated. For a standard, a 1:100,000 solution, prepared from the stock solution, was used. Readings were made on a Bausch and Lomb colorimeter. Approximately 0.2 Gm. (0.051 Gm. for each 100 cc.) was eliminated in the first specimen obtained; by that time 0.4 Gm. had been taken. The second specimen contained 0.23 Gm. in a concentration of 0.052 Gm. for each 100 cc. The last specimen collected in the twenty-four hours contained 0.1 Gm. in a concentration of 0.026 Gm. for each

11. Clark, W. M.: The Determination of Hydrogen Ions, ed. 2, Baltimore, Williams & Wilkins Company, 1923.

100 cc. of urine. The total amount of pyridium eliminated in the twenty-four hours was 0.54 Gm. This was slightly more than half of the total amount taken. For the twenty-four hours following, the urine continued to have the discoloration characteristic of pyridium.

This experiment was corroborated by a second, similar one, in which 0.8 Gm. was taken over a period of twenty-four hours. The three specimens in this instance were pooled, and in the 650 cc. twenty-four hour specimen, 0.41 Gm. of pyridium was eliminated, in a concentration of 0.06 Gm. for each 100 cc. of urine. Again, approximately half the total amount of pyridium taken was eliminated by the urinary route in twenty-four hours. The urine in this experiment was also collected for the succeeding twenty-four hours, and the content of pyridium was calculated from a sample to be 0.04 Gm. From these experiments one can conclude that when pyridium is taken by mouth, essentially half of the amount is excreted in the urine within the twenty-four hours in which it is taken. Owing to its relative insolubility, it is probable that a great portion is lost in evacuations from the bowel.

For estimating the bactericidal abilities of pyridium, Escherichia communior and Staphylococcus aureus were used as test organisms. The strains of organisms were from stock laboratory cultures. Twenty-four hour cultures in plain broth were used throughout the experiments, and both microorganisms had been transplanted daily for ten days before each experiment. Both organisms were found to grow vigorously for at least seventy-two hours in sterile distilled water of a p_H of 6.4; therefore, this was used in making all dilutions of the pyridium and all suspensions of the organisms.

Agar plates, by which both bactericidal and bacteriostatic actions can be noted, were used for the experiments. The stock solution of pyridium was diluted with sterile, triple distilled water to make appropriate concentrations. Portions of 24.5 cc. of the solutions of pyridium were inoculated with 0.5 cc. of a suspension of the organism to be studied. The suspension was made by mixing one part of a twenty-four hour culture with nine parts of triple distilled sterile water. The p_H of the aqueous solution varied from 4.2 to 4.6. At intervals of five minutes, one hour, two hours, four hours and twenty-four hours, 1 cc. samples were taken and placed in sterile Petri dishes. To these plates was added melted beef extract agar (45 to 50 C.) of a rather constant p_H of 6.5. The plates were incubated at 37.5 C. and observed macroscopically and microscopically at the end of twenty-four hours and forty-eight hours, respectively. Between sampling, the flasks were allowed to stand at room temperature (24 C.), since a series of earlier experiments had demonstrated that the action of the drug was not enhanced by incubation temperatures, also that both the organisms

grew vigorously at room temperature. It has been shown that a p_H of from 4.6 to 5.0 inhibits Escherichia communior from growing in urine.[12] Therefore, buffered controls having a p_H corresponding to that of the solutions to be tested were used. These buffered controls were prepared from solutions of sodium phosphate and citric acid.[11] The results are given in detail in table 1. In the 1:1,000 solution, Escherichia communior was killed within five minutes. With one exception, in all of the concentrations from 1:1,000 to 1:7,000, pyridium was bactericidal for Escherichia communior in four hours or less. Bacteriostasis occurred in the same concentrations. Control plates

TABLE 1.—*Bactericidal Action of Pyridium in Solution in Distilled Water on Staphylococcus Aureus and on Escherichia Communior*

Solution of Pyridium		Colonies on Plates* Made from Suspensions of Organisms in Pyridium Solutions That Had Stood for Varying Periods:				
		Staphylococcus aureus				
Concentration	p_H	5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
1:1,000	4.2	70†	65†	194†	3	0
1:2,000	4.4	Innumerable	Innumerable	Innumerable	1,197	17
1:3,000	4.6	Innumerable	Innumerable	2,709	Innumerable	41
1:4,000	4.6	Innumerable	Innumerable	7,560	Innumerable	1,575
1:5,000	4.6	Innumerable	Innumerable	Innumerable	5,481	189
1:6,000	4.5	Innumerable	Innumerable	Innumerable	Innumerable	1,890
1:7,000	4.6	Innumerable	Innumerable	Innumerable	Innumerable	3,780
Control	4.2	Innumerable	Innumerable	Innumerable	Innumerable	0
Control	4.4	Innumerable	Innumerable	Innumerable	Innumerable	0
		Escherichia communior				
1:1,000	4.2	0	0	0	0	0
1:2,000	4.4	26	0	12	0	0
1:3,000	4.6	2	2	2	0	0
1:4,000	4.6	109	1	6	0	0
1:5,000	4.6	126	75	1	0	0
1:6,000	4.5	765	5	126	12	0
1:7,000	4.5	252	1	23	0	0
Control	4.2	Innumerable	Innumerable	Innumerable	Innumerable	0
Control	4.4	Innumerable	Innumerable	Innumerable	Innumerable	0

* The plates were incubated for twenty-four hours.
† These colonies were all counted with a microscope. They are not easily seen macroscopically.

had innumerable colonies except for those made at the twenty-fourth hour. The absence of colonies on the twenty-four hour control plates was apparently due to the acidity of the suspensions from which the plates were partly made, since controls derived from suspensions in plain distilled water (p_H 6.5) had innumerable colonies. A concentration of 1:1,000 was bactericidal for Staphylococcus aureus in between four and twenty-four hours. Bacteriostasis was marked in that concentration. Concentrations of from 1:2,000 to 1:7,000 were not bactericidal for Staphylococcus aureus in twenty-four hours. Slight

12. Clark, W. M.: The Final Hydrogen Ion Concentration of Cultures of Bacillus Coli, J. Biol. Chem. **22**:87, 1915. Michaelis and Marcora, quoted by Clark. Shohl, A. T., and Janney, J. H.: The Growth of Bacillus Coli in Urine at Varying Hydrogen Ion Concentrations, J. Urol. **1**:211 (April) 1917.

bacteriostasis was noted in those concentrations, Briefly, the effectiveness of pyridium as a bactericide was much more marked against the colon bacillus than against the staphylococcus when solutions of the drug in distilled water were used.

Goerner and Haley [13] found that the bactericidal action of pyridium under a somewhat different experimental procedure was evident in concentrations varying between 1 : 4,000 and 1 : 10,000, averaging about 1 : 5,000. The bactericidal action of pyridium for Escherichia communior and Staphylococcus aureus was approximately the same. Stickl,[14] in less extensive experiments with agar plates, using staphylococcus and Eberthella typhi and solutions of pyridium in saline and bouillon, concluded that the action of pyridium against the gram-negative bacilli was much less than against the gram-positive group of bacteria. The differences in antibacterial power as reported by several writers are noteworthy. In all instances, the mediums in which pyridium was permitted to act on the organism and the methods of investigation differed somewhat. Stickl's conclusions were drawn from work with Eberthella typhi. He considered the response of this organism to pyridium as representative of the response of the entire group of gram-negative bacilli. The results of Goerner and Haley did not harmonize with Stickl's findings and conclusions, and would indicate that the bactericidal action of pyridium may be entirely independent of whether the organism is gram-positive or gram-negative. In the experiments herein reported, Escherichia communior was the more sensitive to pyridium in aqueous solutions.

The ideal urinary antiseptic must exert its action in high dilution in the urine. It is therefore essential that experiments in vitro include determinations of the effect of urine on the bactericidal property of pyridium. It is well known that the constituents of urine may markedly modify the bactericidal power of a drug, and that preparations that are of entirely satisfactory bactericidal power when some diluents are present are incapable of destroying the organisms when urine is the diluent. The urine used in this experiment was voided under aseptic conditions by two normal adults, and a complete set of experiments was conducted with the urine of each person (table 2). Two persons were employed to avoid the legitimate criticism that the urine of one might have some peculiar quality that would invalidate the result. Cultures of these specimens, made before pyridium was introduced into the experiments, contained from five to ten colonies of contaminat-

13. Goerner, Alfred, and Haley, F. L.: A Study of the Antibacterial Properties of Pyridium Urinary Antiseptic, J. Lab. & Clin. Med. **16**:957 (July) 1931.

14. Stickl, O.: Untersuchungen über die bakterizide und entwicklungshemmende Wirkung des Pyridiums gegen pathogene Mikroorganismen, Ztschr. f. Desinfekt. u. Gesundhw. **21**:33 (Feb.) 1929.

ing organisms for each cubic centimeter. The urines were diluted with sterile triple distilled water so that the proportions of urine to water in different flasks were 1:9, 2:8, 3:7 and 5:5, but the concentration of pyridium in all flasks and throughout the experiments was 1:5,000. Controls consisted of mixtures of urine and water in the proportion of 1:9, and from the control flasks pyridium was omitted. All flasks were inoculated with Escherichia communior. It was noted that flasks that stood several hours contained crystals in direct proportion to the amount of urine that was used in diluting the stock solution. Microscopically, these crystalline structures were rough, horn-shaped, branching polygons, poorly refractile and with broken edges.

TABLE 2.—*Effect of Urine of Two Normal Adults on Bactericidal* Properties of Pyridium (1:5,000)*

Solution of Urine, Water and Pyridium			Colonies on Plates† Made from Suspensions of Organisms in Solutions of Urine, Water and Pyridium That Had Stood for Varying Periods				
Subject	Proportion of Urine to Water	p_H	5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
1	1:9	5.6–5.8	43	0	0	0	0
2	1:9	5.6–5.8	5	0	0	0	0
1	2:8	5.6–5.8	Innumerable	882	2,016	43	Innumerable
2	2:8	5.6–5.8	4,032	12	18	51	4,536
1	3:7	5.6–5.8	Innumerable	Innumerable	2,331	3,465	Innumerable
2	3:7	5.6–5.8	Innumerable	189	189	315	Innumerable
1	5:5	5.6–5.8	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
2	5:5	5.6–5.8	Innumerable	1,575	2,016	3,024	Innumerable
Control 1	1:9	6.8	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
Control 2	1:9	6.8	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable

* The test organism was Escherichia communior.
† The plates were incubated for twenty-four hours.

The figures (table 2) give evidence of the markedly reduced bactericidal action of pyridium in urine. Under identical experimental conditions and with urine passed by different persons, there was a reduction in the bactericidal action in direct proportion to the amount of urine in the medium in which the organisms grew. In all control specimens the organisms grew vigorously.

Since the action of the dye is in the urinary tract, its value as a urinary antiseptic is more than questionable. Goerner and Haley concluded that urine did not change the bactericidal power of pyridium, but their work was done with agar to which 10 per cent of the urine had been added. From table 2 it can be concluded that such small portions of urine as 1:9, or 10 per cent, do not alter bactericidal ability. Large proportions of urine, however, do lower the bactericidal powers to an extent that allows the organism to grow uninhibited. These experiments in which large proportions of urine were used are, of

course, more comparable to the process in vivo. Also, the method that permits constant contact of pyridium with urine in fluid medium before culture, rather than contact only at the time of making the plates, seems preferable.

There still remained one question to be answered. Is pyridium, taken by mouth and excreted in the urine, bactericidal? The specimens obtained during the time the drug had been taken by mouth for colorimetric determinations had been collected by the aforementioned aseptic method; therefore, dye in concentrations of from 1:1,600 to 1:2,400 was available for examination. Determinations of the p_H of specimens before and after taking the drug by mouth showed little if any change. Portions of 25 cc. in sterile flasks were inoculated with 1:100 suspensions of the pathogenic organisms by use of a platinum needle. This method of inoculation reduced the number of organisms placed in the

TABLE 3.—*Bactericidal Action of Pyridium as Excreted in the Urine*

Organisms	Concentration of Dye in Urine	p_H of Urine and Dye or of Urine Only	Colonies on Plates Made Either from Specimens of Inoculated Urine That Contained Dye When Passed or from Inoculated Urine Only, Which Had Stood for Varying Periods				
			5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
Escherichia communior.....	1:1,600	6.4	252	252	281	294	Innumerable
Escherichia communior (control)	No dye; urine only	6.3	252	173	176	189	Innumerable
Staphylococcus aureus.....	1:1,600	6.4	567	630	630	630	945
Staphylococcus aureus (control)	No dye; urine only	6.3	66	72	62	62	Innumerable

urinary solution of the dye and facilitated the counting of colonies and observations of the trend of growth. Controls were made from specimens eliminated just before the dye had been administered by mouth. The tendency to inhibition of growth of staphylococcus was noted (table 3). This is evident particularly in the column in table 3 that represents results after twenty-four hours. Nevertheless, the effect was evident throughout, for although the number of colonies of the Staphylococcus aureus control and of Escherichia communior were less, the number of organisms in the original suspensions was also less. That this difference in the number of organisms in the original suspensions actually existed can be verified by a glance at the column headed "five minutes," for during such a short period neither growth nor inhibition of growth could have progressed sufficiently to change the original number of viable organisms materially.

Similar experiments with staphylococcus were made in samples of urine containing the drug in concentrations of 1:1,800 and 1:2,400, respectively. In the more concentrated of the two specimens, some inhibition of growth of staphylococcus was still present, but inhibition

was less marked than in the specimen in which the concentration of the drug was 1:1,600. In the specimen of concentration 1:2,400, the ability to inhibit had been lost, and twenty-four hour cultures contained innumerable colonies. The inhibitory action on staphylococcus of urinary solutions of pyridium is probably lost in concentrations of less than 1:2,000. It should be emphasized that this effect on Staphylococcus aureus is bacteriostatic and not bactericidal. This would substantiate the observations of Köster.[15] Thomas and Wang,[16] in a study of sixty specimens of urine that contained pyridium, however, found only six that had any antiseptic property against staphylococcus. In my experiments the colon bacillus grew vigorously in a concentration of 1:1,600. While watery solutions of pyridium were more effectual against Escherichia communior than against staphylococcus, the reverse is true when urine that contains the dye following administration by mouth is used. With specimens obtained from three normal persons who had taken 0.2 Gm. of pyridium three times daily, it has been found impossible to obtain inhibition of growth, or to kill Escherichia communior when that organism was placed in samples of the urine.[17] It appears conclusive from experimental evidence that treatment by pyridium of infections of the urinary tract with Escherichia communior will be ineffective. In infections with staphylococcus, suitable concentrations of pyridium may exhibit some slight bacteriostatic effect, but probably will not alone be effectual in eliminating the invader. To obtain these bacteriostatic concentrations, it seems that larger doses of the drug than those advocated by the manufacturers would be necessary.

In experimental work there was some evidence that would lead one to believe that pyridium administered by mouth is changed in passage through the body and urinary tract. It was noted in this experiment and by others[13] that attempts to dilute concentrated solutions of pyridium (1:2,000 or more) with urine produced a heavy, amorphous, orange-yellow precipitate. However, the drug can be excreted in the urine without precipitate in concentrations from which this precipitate invariably is brought down when the same concentrations are made in vitro from stock solutions and urine. Excreted specimens contain no precipitate even on standing forty-eight hours. This would point to some change in the character of the drug by passage through the body. Further, it was noted that in higher dilutions of pyridium containing a proportion of urine, although precipitate did not form, crystals

15. Köster, O.: Bakteriologische und klinische Versuche mit Pyridium, München. med. Wchnschr. **1**:1013 (June 13) 1930.

16. Thomas, B. A., and Wang, I. K.: Studies on the Comparative Clinical Values of Various So-Called Urinary Antiseptics, J. Urol. **22**:22 (July) 1929.

17. Helmholz, H. F.: Unpublished data.

appeared on standing. The amount of these crystals was in direct proportion to the proportion of urine present. Although not conclusive, such observations are suggestive that pyridium administered by mouth is altered chemically before elimination.

It has been reported by others that blood serum does not alter the bactericidal property of pyridium. The experiments referred to differed from those on which this report is based, in that the suspension of organisms in liquid agar and serum was not added to the solution of pyridium until the time for making the plates. It is possible that the changes observed by me in a liquid medium that more nearly approximated conditions in vivo will not occur in the solid agar plates. Since experiments with urine in vitro disclosed a marked reduction of the bactericidal ability, the conclusion that blood serum did not alter this quality seemed open to investigation. From the stock solution three

TABLE 4.—*Effect of Normal Blood Serum on the Antibacterial Property of Pyridium Against Escherichia Communior*

Aqueous Solution of Pyridium	Added Substance	p_H of Final Solution	Colonies in Plates Made from the Various Suspensions Which Had Been Allowed to Stand for Various Periods				
			5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
1:7,000	None	4.6	53	4	1	1	0
1:7,000	10 per cent human serum	...	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
1:7,000	20 per cent human serum	...	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
Control	Sodium phosphate and citric acid	4.6	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable

aqueous solutions containing pyridium in a concentration of 1:7,000 were prepared. These three separate portions, of a concentration of 1:7,000, differed from each other only in the fact that one was made up entirely by dilution with distilled water, another with water and 10 per cent of blood serum of man and a third with water and 20 per cent of serum. The method of inoculation and incubation employed in this experiment was identical with that in experiments in which watery solutions were used. The control was a buffered solution with a p_H of 4.6. It was noted that the portions containing serum became somewhat hazy and more yellowish on standing an hour.

Growth was abundant in both flasks containing blood serum as well as in the control (table 4). The effect of the plain aqueous solution was bactericidal. It was concluded that blood serum plays a part similar to urine in altering pyridium, so that its bactericidal and bacteriostatic qualities are lost.

Summary.—Approximately 50 per cent of a portion of pyridium that is administered by mouth is excreted in the urine within twenty-

four hours. Small amounts of the dye are eliminated by the urinary route for several hours following the first twenty-four. With comparative ease, by restriction of the intake of fluid, concentrations of from 1 : 1,600 to 1 : 2,400 may be attained when the dose is from 0.8 to 1 Gm. daily.

Experiments in vitro indicate that the bactericidal action of pyridium in aqueous solutions and under the conditions followed in the experiment is much greater against the colon bacillus than against Staphylococcus aureus. In concentrations of from 1 : 1,000 to 1 : 7,000, aqueous solutions are bactericidal for colon bacillus within four hours. Such concentrations, with the exception of 1 : 1,000, are ineffective for Staphylococcus aureus in from twenty-four to forty-eight hours.

The addition of urine to watery solutions of the drug causes a striking reduction in the bactericidal properties. The growth of organisms and reduction of bactericidal ability are directly proportional to the amount of urine contained in the solution. Urine containing the excreted dye in concentrations of 1 : 1,600 and 1 : 1,800 following administration by mouth has a slight bacteriostatic but not a bactericidal effect on Staphylococcus aureus. There is no tendency either to inhibit or to kill Escherichia communior in these concentrations, and they grow vigorously. Normal blood serum also reduces the antibacterial qualities of pyridium in vitro.

Evidence is presented that suggests that pyridium administered by mouth is changed in passage through the body, and the dye excreted in the urine is not pyridium.

SERENIUM

Another proprietary preparation on the market has been used considerably as a bactericide for infections of the genito-urinary tract. Serenium is a chemical compound, an organic dye, the hydrochloride of 2-4 diamino 4′ ethoxyazo benzene. It is advocated as a relatively nontoxic compound, excreted almost exclusively in the urine. According to the manufacturers, when the daily dose is three tablets, its concentration in the urine is approximately 1 : 5,000. The drug has been advocated for pyelitis and cystitis. Also it is claimed that administration over a period of only five or six days will sometimes be sufficient to clear up the symptoms and clinical manifestations, but that it is best to continue the administration for at least two weeks after the cessation of symptoms, in order to prevent relapse. It is claimed to have bacteriostatic properties in acid urine, and since urine is normally slightly acid it is therefore of suitable reaction. The drug imparts a deep orange or reddish color to the urine and exhibits marked staining qualities. Reports of clinical results obtained with the drug are not available in the literature so far as I could find. In a number of

infections of the urinary tract observed at the Mayo Clinic, in which serenium had been used as a therapeutic agent, the results were not promising. These were infections of the upper part of the urinary tract and cases of cystitis in which cultures of the urine contained such common pathogenic organisms as Escherichia communior and staphylococcus. However, the number of cases was too small to allow of well formed clinical conclusions as to its therapeutic value.

To determine the amount of serenium excreted in the urine when the drug is ingested, tablets of 0.1 Gm. were utilized. A sterile specimen of urine was collected just prior to the administration of the drug and was reserved for controls in bactericidal tests. Two tablets of 0.1 Gm. were taken every six hours for four doses. It will be noted that this exceeds the recommended dose of 0.3 Gm. daily. The intake of fluids was moderately reduced. Comparisons were made on a colorimeter, using as a standard a 1 : 10,000 alcoholic solution of serenium. Serenium, although extremely insoluble in plain distilled water, is easily dissolved in ethyl alcohol, giving a clear wine-red solution. By the same colorimetric method and formula used in the experiments with pyridium, 0.075 Gm. of serenium was found to be excreted in the twenty-four hour specimen of urine, in a concentration of 0.015 Gm. for each 100 cc. The amount excreted in the second twenty-four hours was very slight, being calculated as 0.005 Gm. It is evident that the serenium eliminated is but a small fraction of that ingested. Following the administration of 0.8 Gm., only 0.07 Gm. was eliminated in the urine during the twenty-four hours within which the drug was taken. This small fraction eliminated in the urine is explained, no doubt, by the extreme insolubility of the drug. It is probable that considerable serenium is passed in intestinal evacuations before it can be dissolved and absorbed. Urinalysis of the specimens following the ingestion of serenium failed to show any evidence of renal irritation. One specimen collected during the first twenty-four hours was calculated by colorimetric methods to contain serenium in concentrations of 1 : 4,000, and was reserved for tests of bactericidal powers.

To verify the previous experiment regarding the elimination of ingested serenium, the drug was administered to three normal adults. The first subject took 1 Gm. by mouth in doses of 0.2 Gm. every four hours, over a period of twenty hours. The serenium in specimens collected during the twenty hours varied in concentrations of from 1 : 5,000 to 1 : 35,000. The total amount of drug excreted in twenty-four hours was 0.04 Gm. A second subject ingested 0.8 Gm. of serenium in twenty-four hours. Two tenths gram was administered at intervals of approximately six hours. The concentration in the urine varied from 1 : 7,000 to 1 : 100,000. The total amount of serenium eliminated

in that time was 0.07 Gm. The third subject took 0.8 Gm. of serenium in twelve hours, and in specimens collected during that time the concentration was from 1 : 10,000 to 1 : 16,000. The total amount of drug eliminated in the twelve hours was 0.02 Gm. From the first subject sterile specimens containing serenium in a concentration of from 1 : 8,000 and 1 : 16,000, respectively, were collected and reserved for bacteriologic studies. Even with a marked restriction of the intake of fluid, concentrations as great as 1 : 4,000 were not again obtained, and it should be concluded that concentrations of 1 : 5,000 or greater are rarely obtained. Restriction of the intake of fluids is essential for obtaining such concentrations as those mentioned. The amount eliminated is a small fraction of that ingested. Specimens after twenty-four hours not infrequently contained gross traces of the drug, but the concentrations were very small. Ingested serenium does not alter the p_H of the urine.

Serenium powder, provided by the manufacturers, was used in making the alcoholic standard and aqueous solutions for bactericidal determinations. The drug, even in powder form, is extremely insoluble, and it was not possible to prepare a concentrated stock solution with distilled water. Heat was ineffective in dissolving the drug. A 1 : 5,000 solution was prepared by grinding the powdered drug in a mortar and dissolving it with the aid of a few drops of tenth-normal hydrochloric acid. Sterile distilled water and enough tenth-normal sodium hydroxide to neutralize the acid that had been added was used to make the solution up to volume. Even then the solution contained some fine suspended particles; so it was filtered. This clear, wine-red, filtered solution was compared colorimetrically with the 1 : 10,000 alcoholic standard solution of serenium. The concentration of the drug in the solution tested was calculated to be 1 : 6,000. The solution that had been prepared in a concentration of 1 : 5,000 was then actually a 1 : 6,000 solution owing to incomplete solubility of serenium. The p_H of the solution of serenium, as determined by the quinhydrone electrode method, was markedly acid, as shown in table 5.

For determining the bactericidal action of serenium in distilled water, the 1 : 6,000 concentration was used, and less concentrated solutions were made by dilution with distilled water. Controls were buffered solutions. The general technic and procedures were identical with those employed in the experiments with pyridium.

Between samplings, the inoculated flask stood at room temperature, since earlier experiments, whether with or without incubation of solutions of serenium, gave essentially the same results. The antibacterial properties of serenium were not enhanced by incubation; moreover, the bacteria flourished at room temperature.

All aqueous solutions of serenium (table 5) in concentrations of from 1:6,000 to 1:14,000 were actively bactericidal for Escherichia communior in twenty-four hours and practically so in four hours. In concentrations of 1:6,000 and 1:8,000, the bactericidal action was complete in between five minutes and one hour. In none of the plates made at the end of twenty-four hours was there growth. The effect on staphylococcus was less marked. Bacteriostasis occurred, but the

TABLE 5.—*Bactericidal Action of Serenium in Solution in Distilled Water on Escherichia Communior and on Staphylococcus Aureus*

Solution of Serenium, Concentration	p_H	Colonies on Plates Made from the Various Suspensions, Which Had Been Allowed to Stand for Various Periods				
		Escherichia communior				
		5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
1:6,000	4.4	2	0	0	0	0
1:8,000	4.8	5	0	0	0	0
1:10,000	4.8	9	2	1	0	0
1:12,000	4.8	131	6	1	1	0
1:14,000	4.9	58	17	2	1	0
Control	4.4	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
Control	4.8	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
		Staphylococcus aureus				
1:6,000	4.4	Innumerable	5,796	1,512	102	0
1:8,000	4.8	Innumerable	Innumerable	630	441	0
Control	4.4	Innumerable	Innumerable	Innumerable	Innumerable	0
Control	4.6	Innumerable	Innumerable	Innumerable	Innumerable	0

TABLE 6.—*Effect of Urine on the Bactericidal Properties of Serenium on Escherichia Communior*

Solution of Serenium			Colonies on Plates Made from the Various Suspensions, Which Had Been Allowed to Stand for Various Periods				
Concentration	Proportion Urine to Water	p_H	5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
1:12,000	4.8	All water	73	0	1	1	0
1:12,000	6.1	1:3	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
1:12,000	6.1	2:2	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable
Control	4.8	All water	Innumerable	Innumerable	Innumerable	Innumerable	Innumerable

killing noted in twenty-four hours could not be attributed to the drug, since the controls were also negative.

A solution containing serenium in concentrations of 1:6,000 was diluted to make the appropriate concentration of 1:12,000. Three 24.5 cc. portions of concentrations of 1:12,000 were prepared, differing from each other only in the fact that in one the dilution was made with sterile water only, in another with one part of urine and three parts of water, and in a third with two parts of urine and two parts of water. Escherichia communior was the test organism (table 6). The control was made from a buffered solution of p_H 4.8. The

1 : 12,000 solutions and the controls were inoculated with 0.5 cc. of 1 : 10 suspension of Escherichia communior.

In the flasks containing urine, the color of the solutions changed from wine-red to a somewhat lighter, hazy red. This resembled a similar change noted in urine containing solutions of pyridium. The marked loss of bactericidal power was striking. A plain, aqueous solution of serenium had previously demonstrated bactericidal properties, but both solutions containing urine completely lost any such qualities. Hardly any happening but a chemical alteration in the drug would explain the instant and complete loss of antibacterial properties.

For an estimation of the bactericidal powers of serenium excreted in the urine, the 1 : 4,000, 1 : 8,000 and 1 : 16,000 specimens collected with sterile precautions when the drug had been taken by mouth were used. Controls were made from plain urine collected aseptically. By

TABLE 7.—*Bactericidal Action of Serenium as Excreted in the Urine*

Organism	Concentration of Dye	*p*H of Solution	Colonies on Plates Made from the Various Suspensions, Which Had Been Allowed to Stand for Various Periods				
			5 Minutes	1 Hour	2 Hours	4 Hours	24 Hours
Escherichia communior.....	1:4,000	6.0	51	79	64	65	2,898
Escherichia communior.....	1:8,000	6.2	207	239	315	233	Innumerable
Escherichia communior (control)	No dye; urine only	6.3	378	630	756	998	Innumerable
Staphylococcus aureus.....	1:4,000	6.0	69	54	55	49	44
Staphylococcus aureus.....	1:8,000	6.2	239	144	252	195	226
Staphylococcus aureus.....	1:16,000	6.3	270	214	252	315	220
Staphylococcus aureus (control)	No dye; urine only	6.3	378	756	693	882	Innumerable

means of a platinum needle, 25 cc. portions were inoculated with pathogenic organisms in 1 : 100 suspension in distilled water. On standing, the solutions showed neither change in color nor tendency to form crystals.

The marked bacteriostatic effect of all tested concentrations on staphylococcus could be noted (table 7). Even after twenty-four hours this ability to inhibit growth had not been lost. Bactericidal qualities were not demonstrated. Bacteriostasis against colon bacillus occurred in a concentration of 1 : 4,000, but began to diminish between the fourth and the twenty-fourth hours. However, at the twenty-fourth hour slight bacteriostasis was still evident. There was no bacteriostasis of Escherichia communior by a 1 : 8,000 concentration of the drug. Control plates of both Escherichia communior and staphylococcus contained innumerable colonies on the twenty-fourth hour. With regard to Staphylococcus aureus, the drug had merit as a bacteriostatic agent. It had inhibiting effects on Escherichia communior only in a concentration (1 : 4,000), that is rarely obtained when the drug is taken by

mouth and then only with increased doses. A bactericidal effect should not be expected when either of the two tested organisms is the offender.

Summary.—Serenium is an extremely insoluble drug. It is readily excreted in the urine, but in amounts much less than those ingested. No doubt a considerable part of the ingested dose is eliminated by bowel before solution and absorption can occur. With restriction of the intake of fluids, a concentration of 1:4,000 was attained on one occasion. Greater concentrations by further restriction seem of unlikely possibility. The experiments herein reported indicate that concentration, with the dosage as given, and moderate restriction of the intake of fluid will vary from 1:10,000 to 1:16,000; higher dilutions are frequent.

Solutions of serenium in distilled water, in concentrations of from 1:6,000 to 1:14,000, are actively bactericidal for Escherichia communior. Similar solutions in concentrations of 1:6,000 and 1:8,000 are bacteriostatic but not bactericidal for Staphylococcus aureus. The absence of colonies of staphylococci on twenty-four hour plates cannot be attributed to the drug, since twenty-four hour control plates were likewise negative.

When urine is used in making dilutions of serenium, the antibacterial properties of the drug are entirely lost as regards Escherichia communior. A change in the appearance of these urine-containing solutions on standing and the complete loss of antibacterial qualities suggest a chemical reaction between the drug and some urinary constituent. Since serenium excreted in the urine causes no such change, it might be postulated that the drug is chemically altered in its passage through the body. Serenium excreted in the urine in concentrations of 1:4,000, 1:8,000 and 1:16,000, when the method is that used in this procedure, is actively bacteriostatic for staphylococcus. The 1:4,000 concentration is slightly bacteriostatic for Escherichia communior; the 1:8,000 concentration is not. No bactericidal effect on either organism was noted.

GENERAL SUMMARY AND CONCLUSIONS

Antisepsis in urine is quite different from antisepsis in water. Compounds that exert a striking bactericidal action in water may have this power greatly diminished or lost in urine. This well recognized fact has excluded many drugs from the list of valuable urinary antiseptics. The value of every drug used for urinary antisepsis ought to be questioned until this antiseptic strength in urine can be experimentally demonstrated. Compounds, the antiseptic power of which is due to acid or basic properties, would become inert in the urine owing to the buffer action of urinary salts. Other compounds containing silver become inert in the urine because silver is precipitated by the

chlorides. A large number of drugs, according to Davis, lose their antiseptic action owing to some as yet unknown interfering action. From the experiments here reported the reduction or loss of antiseptic action in urine of these two chemotherapeutic drugs falls in the class of an unknown interfering action. It has been suggested from rather meager "test tube" observations that a chemical alteration of the compounds by urinary constituents may account for such a loss.

The antibacterial action of the two compounds investigated was quite independent of the gram-staining quality of the organisms used. In aqueous solutions both showed a decidedly greater effectiveness against Escherichia communior. The excreted drugs, however, showed an ability to inhibit the gram-positive organisms when Escherichia communior grew vigorously. Antibacterial powers of the drugs are influenced, then, to a great extent by the mediums in which they are permitted to act on the organism.

Both pyridium and serenium were eliminated in the urine in quantities that caused a marked discoloration of the urinary stream. Pyridium was eliminated in the urine in rather high concentrations, but these concentrations failed to effect bacteriostasis of the colon bacillus. Serenium in a concentration of 1:4,000 did cause a moderate inhibition of Escherichia communior. However, this concentration, which effected the bacteriostasis of Escherichia communior, rarely can be obtained. The concentrations usually obtained had no inhibitory action on Escherichia communior. Both drugs excreted in sufficient concentrations are bacteriostatic for Staphylococcus aureus. No bactericidal effect was noted with either drug in any of the concentrations in urine in which they were obtained in this experiment. It does not seem that the recommended doses of 0.2 Gm. and 0.1 Gm., respectively, given three times daily, even with a restriction of the intake of water, would attain a concentration sufficient even to inhibit Staphylococcus aureus. Also, from these experiments it does not appear probable that even with large doses benefit will be derived from such clinical treatment of genito-urinary infections due to the resistant colon bacillus.

The problem has been entirely experimental. No clinical conclusions as to the sedative action of the drugs, their ability to clear the urine of pus, or their effect on organisms other than the two tested have been reached. It has been definitely shown by these procedures that the value of these agents in genito-urinary infections is limited, that their antiseptic properties are lost or reduced in urine, and that clinical improvement, as judged by cultures of the urine, is not to be expected when Escherichia communior is the offending organism.

EXCRETION OF XYLOSE AS A MEASURE OF RENAL FUNCTION IN CHILDREN

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The elimination through the kidney of a fixed proportion of ingested or parenterally administered pentose sugars, combined with the extremely low threshold of the kidney membrane for these sugars, would seem to indicate their use as a delicate measure of renal function. Up to this time, such a use has not been feasible owing to the extremely high cost, but the recent development of a method for the cheap production of xylose has rendered that substance available for this purpose. One thus is enabled to judge the functional power of the kidney by a simple quantitative determination of the reducing-power of the urine two hours after ingestion. Somogyi's [1] simple method for the determination of a nonfermentable reducing substance in the blood in the presence of dextrose by the substitution of a yeast suspension for the water used in the Folin-Wu tungstic acid precipitation in the determination of the blood sugar allows the estimation of the amount of xylose circulating in the blood at any moment after the ingestion of the pentose. This enables one to measure the functional power of the kidney even in the absence of urine, a matter of paramount importance, especially in infants in whom the regular collection of specimens of urine is particularly difficult.

The question as to the amount of pentose sugar actually utilized has long been a subject of controversy. It is now the consensus that it cannot be assimilated and that it passes through the liver unchanged, to be excreted in the urine or broken down by the intestinal bacteria. It has been shown by us [2] in a series of animal experiments that in the rabbit, when the liver has been damaged by phosphorus, the assimilation of galactose (a sugar which is converted into glycogen in the liver to a large percentage, and may even be used to allay the effects of insulin shock) is definitely disturbed and that the galactose circulates in the blood stream as such for a much longer period than in the normal ani-

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From the Chemical Laboratory of the Beth Israel Hospital.

1. Somogyi, M.: Reducing Non-Sugars and True Sugar in Human Blood, J. Biol. Chem. **75**:33 (Oct.) 1927.

2. Fishberg, E. H., and Friedfeld, L.: The Excretion of Xylose as an Index of Renal Function, J. Clin. Investigation **11**:501 (May) 1932.

mal. These animals show a curve of nonfermentable reducing substance in the blood which, instead of bending downward from a three hour maximum, continues upward for many hours. Such animals show no deviation from the normal curve on the ingestion of xylose. If, however, such an animal is poisoned by uranium, so that there is definite necrosis of the membrane of the kidney, a long delay in the disappearance of xylose from the blood becomes manifest. These same facts were clinically noted in a case of acute yellow atrophy of the liver due to cinchophen poisoning; the nonfermentable reducing substance of the blood showed a normal curve after the ingestion of xylose, while that of galactose was entirely disturbed. For all practical purposes, the nonparticipation of the liver in the metabolism of xylose may be assumed. Actually, this question is eliminated from our problem, since the results in normal subjects are so constant, while those showing impaired kidney function deviate so consistently, that only the relative values will enter into our work.

The normal nonfermentable reducing substance of the blood is equal to 28 mg. per hundred cubic centimeters, and this figure is remarkably constant. On ingestion of 1 Gm. of xylose per 3 pounds (1.4 Kg.) of body weight up to a maximum of $^{15}/_{50}$ Gm., the concentration of the nonfermentable reducing substance of the blood rises within three hours to reach a maximum of about 80 mg., and then falls to a value around 45 mg. within five hours. It has been found by one of us (Dr. Fishberg [3]) that xylose injected into the blood stream disappears at a rate proportional to the actual momentary concentration of nonfermentable reducing substance in the blood; hence this rate will grow slower as the actual amount decreases, and the restoration of the normal figure during fasting will be slow.

Any normal subject on the ingestion of the amount of xylose mentioned in the last paragraph within twenty-four hours will excrete 25 per cent of the total given, plus or minus 5 per cent. Thus a normal adult will excrete within twenty-four hours from 10 to 14 Gm. A child weighing 75 pounds (34 Kg.) after taking 25 Gm. will excrete from 5 to 7 Gm. Within two hours after ingestion the concentration of reducing substance in the urine as determined by the Benedict sugar method will be above 2.5 per cent. This point is of paramount importance in judging the functional impairment of the kidney since the ability to concentrate is the best measure of functional integrity which is at present available. The amount excreted during twenty-four hours is practically independent of the amount of fluid given, and the regulating power of the kidney has been found so fine that there is an equal amount of pentose sugar excreted in 4,500 cc. and in 200 cc. of urine, provided the kidney is functionally intact. In fact, the number of

3. Fishberg, E. H.: The Rate of Disappearance of Foreign Sugar from the Blood Stream, J. Biol. Chem. **86**:665 (April) 1930.

grams per hour is independent of the amount of fluid. The extrarenal factors play a smaller rôle in the xylose test than in many of the other kidney function tests heretofore in use. In a case of cirrhotic carcinoma of the liver in which 9 liters of ascitic fluid was removed, a normal xylose curve was found in the blood.

TECHNIC

After limiting the intake of fluids from the preceding evening, specimens of blood and urine are taken in the morning. One gram of xylose per 3 pounds of body weight, up to a maximum of 50 Gm., is given in lemonade. Specimens of blood are collected at one and one-half, three and five hours. Specimens of urine are taken at one, two, five, eight and twelve hours, and then another twelve hour specimen. Quantitative reduction tests are made on the specimens of urine.

One cake of Fleischmann's yeast is shaken with ten times the volume of water and centrifugated. The supernatant fluid is poured off, and this process is repeated until the supernatant liquid no longer shows any reducing power with a Benedict solution. A 10 per cent solution of this yeast is then made. One cubic centimeter of oxalated blood is dropped into 7 cc. of this solution and allowed to stand two minutes. Two cubic centimeters of tungstic acid is then added, and the Folin-Wu determination of reducing substance done.

In the event of functional impairment of the kidney, there is a marked variation in the xylose metabolism. In the blood, instead of the curve of the nonfermentable reducing substance approaching normal after five hours, the concentration stays high so that there may be 100 mg. or even more. As recovery proceeds, the curve bends down until the normal form is again restored. This shape of the curve is not accidental, because in patients who are unable to retain all of the xylose, owing to uremic vomiting, it is found that the curve goes steadily upward in the same fashion, even though the actual values reached are not as high. A normal subject on ingesting the same amount of xylose as is retained by these nephritic patients shows the characteristic normal parabola curve.

The kidneys of nephritic patients cannot concentrate xylose in the urine within two hours to the 2.5 per cent value established as the minimum normal in functional integrity of the kidney. The kidney in severe cases cannot concentrate at all, and values as low as the xylose concentration in the blood are encountered, i. e., a concentration of 0.1 per cent or even less. The total output per day is much lowered, and instead of 25 per cent of the total amount given being excreted, perhaps 5 per cent or even less is excreted. How far the values lying between these two extremes are a quantitative estimate of the number of functional intact renal units (a glomerulus with its accompanying tubule) will have to be determined.

The following cases are fairly typical of the applications of the xylose test.

REPORT OF CASES

CASE 1.—S. P., aged 11, weighing 74 pounds (33.6 Kg.), and having a blood pressure of 130 systolic and 90 diastolic, had had "kidney trouble" six years previously. The mother had the child admitted to the hospital because of beginning swelling of the face and hematuria.

Urinalysis revealed: reaction, acid; albumin, a trace; dextrose, 0; acetone, 0; red blood cells, rare; occasional white blood cells; specific gravity, 1.020. Examination of the blood showed: 4,200,000 red cells and hemoglobin, 65 per cent. The results of the xylose test of the blood and urine follow:

Blood		Urine			
Time, Hours	Nonfermentable Reducing Substance, Mg./100	Time, Hours	Cc.	Per Cent	Gm.
0	28	1	23	1.1	0.3
1½	67	2	31	2.5	0.8
3	78	5	140	2.5	3.4
5	41	8	104	1.2	1.2
		12	45	0.8	0.3
		24	133	0.2	0.2
		Total	476		6.16

From the blood curve and the fact that the concentration of nonfermentable reducing substance in the urine reached 2.5 per cent within two hours and that over 25 per cent of the total given was excreted within twenty-four hours, the functional integrity of the kidney can be affirmed. Further examination showed the presence of rheumatic fever.

CASE 2.—B. L., aged 13, was admitted to the hospital with the history of pain in the left upper quadrant of the abdomen for five or six months, pain in the small of the back for four months, vomiting for four months and headache for four days. There had been dizziness, difficult vision, convulsions and stupor. During laparotomy a hard, nodular pancreas had been noted. The child was admitted in convulsions simulating epilepsy.

Roentgenograms showed marked osteolysis of all bones. Urinalysis showed: specific gravity, from 1.013 to 1.016; Bence Jones reaction, 0; red blood cells, 0; white blood cells, occasional; epithelial cells, few. Examination of the blood showed: red blood cells, 2,850,000; hemoglobin, 56; carbon dioxide, 74.5; dextrose, 100 mg.; nonprotein nitrogen, 31.5 mg.; calcium, 9.2 mg.; lipins, 970 mg.; phosphorus, 3.2 mg.; phosphate, 3.2 mg., and cholesterol, 210 mg. per hundred cubic centimeters, respectively. The results of xylose tests of the blood and urine follow:

Blood		Urine			
Hours	Nonfermentable Reducing Substance, Mg./100	Time	Volume	Per Cent	Gm.
0	28	9-10	56.8	0.23	0.13
1½	51	10-11	70.8	0.65	0.46
3	63	11- 2	212.0	0.45	0.95
5	71	2- 4:30	280.0	0.30	0.84
		4:30- 5	59.3	0.13	0.84
		5- 8	152.0	0.09	0.13
		8- 8	604.0	0.00	0.00
		Total	1,434.9		2.58

The diagnosis was multiple myeloma. The maximum concentration of xylose of 0.65 per cent in the urine and the total output of 2.58 Gm. in twenty-four hours, instead of the normal, from 12 to 14 Gm., show severe impairment of renal function.

CASE 3.—H. K., aged 9, weighing 62½ pounds (28.35 Kg.), with a blood pressure of 110 systolic and 70 diastolic, was admitted to the hospital with the history

of vomiting for one week, loss of 6 pounds (2.7 Kg.) during the preceding month, and anemia. This attack dated back to a similar one the previous year. The child's urine had shown albumin since that time. He had been well up to six days before admission, when he vomited food, solids or liquids. The breath had the odor of urine. He had been lethargic for a year. There had been no edema or eruption.

Urinalysis showed: specific gravity, 1.008; a few hyaline casts; occasional red blood cells; many white blood cells, and pus cells. Examination of the blood revealed: red blood cells, 2,800,000; total protein, 7.20 per cent; carbon dioxide, 60; dextrose, 121 mg.; urea nitrogen, 80 mg.; nonprotein nitrogen, from 150 to

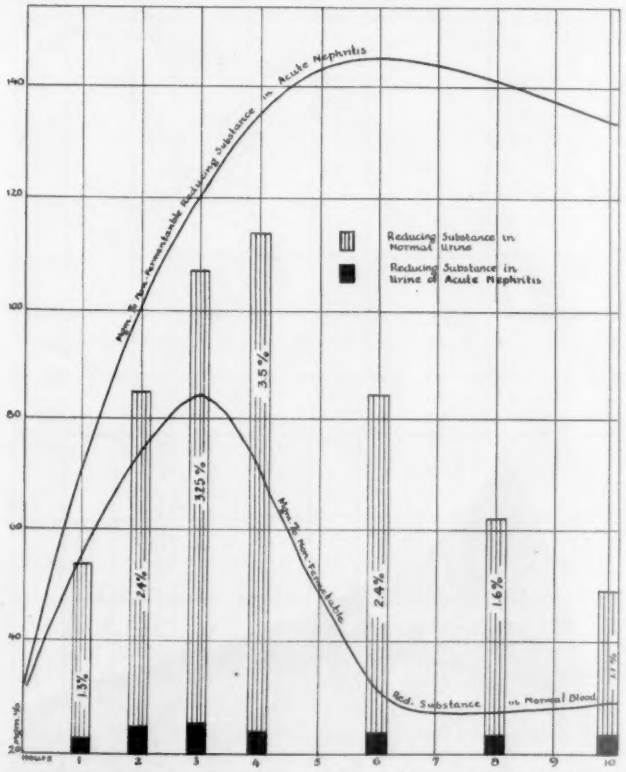

Chart 1.—The percentage of nonfermentable reducing substance in normal urine and in urine of acute nephritis.

120 mg.; creatinine, 6 mg.; cholesterol, 160 mg.; chlorides, 580 mg.; calcium, 9 mg., and phosphorus, 12 mg. The results of the xylose tests of the blood and urine follow:

Blood		Urine			
Hours	Nonfermentable Reducing Substance, Mg./100	Time	Cc.	Per Cent	Gm.
0	28	9-10	10.0	0.0	0.0
1½	43	10-11	9.0	0.0	0.0
3	69	11-12	28.8	0.0	0.0
5	79	12- 2	51.0	0.0	0.0
		2- 5	0.0	0.0	0.0
		5- 8	87.0	0.1	0.1
		8- 8	45.0	0.0	0.0
Total			230.8		0.1

These results show severely impaired renal function.

CASE 4.—M. C., aged 10½ years, weighing 95 pounds (43.1 Kg.), was admitted to the hospital complaining of an illness that had begun sixteen days before, with frontal headaches and fever. At the same time, the child's brother had become ill with suppuration of the ear and acute nephritis. Four days before admission the temperature was 106.6 F. There was slight epistaxis, and the glands of the neck were swollen. Nocturia was present one or two times. The child drank a great deal. Hematuria was observed, and there was a slight swelling of the face.

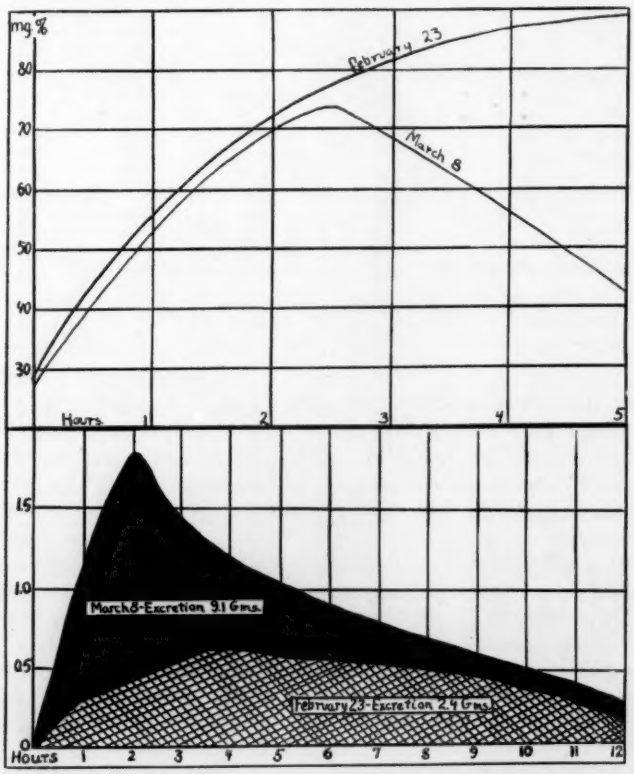

Chart 2.—The concentration of nonfermentable reducing substance in the blood (upper graph) and urine (lower graph) in acute nephritis after the ingestion of 35 Gm. of xylose.

The blood pressure was 120 systolic and 70 diastolic. A petechial rash was apparent.

On February 23, urinalysis showed: specific gravity, 1.004; albumin, a trace; dextrose, 0; acetone, 0; occasional granular casts; many red blood cells; many white blood cells and many epithelial cells. The benzidine reaction was 4 plus. Examination of the blood revealed: red blood cells, 3,850,000; leukocytes, 14,800; dextrose, 110; urea nitrogen, 13 mg.; nonprotein nitrogen, 28.5 mg.; creatinine, 1.3 mg.; cholesterol, 160 mg.; total protein, 4.68 Gm., and albumin, 2.34 Gm.

On March 8, urinalysis showed: specific gravity, 1.010; albumin, 2 plus; casts, 0; red blood cells, few; epithelial cells, many, and benzidine reaction, 1 plus. The temperature was normal.

Chart 2 shows the results of the xylose test on February 23 and March 8. It can be seen that at first the function was generally impaired, and that with the restoration of function the normal values for the excretion of xylose again appeared.

Chart 3 shows the blood curves of three infants whose urine could not be obtained: a normal infant of 8 months, a child that was anuric

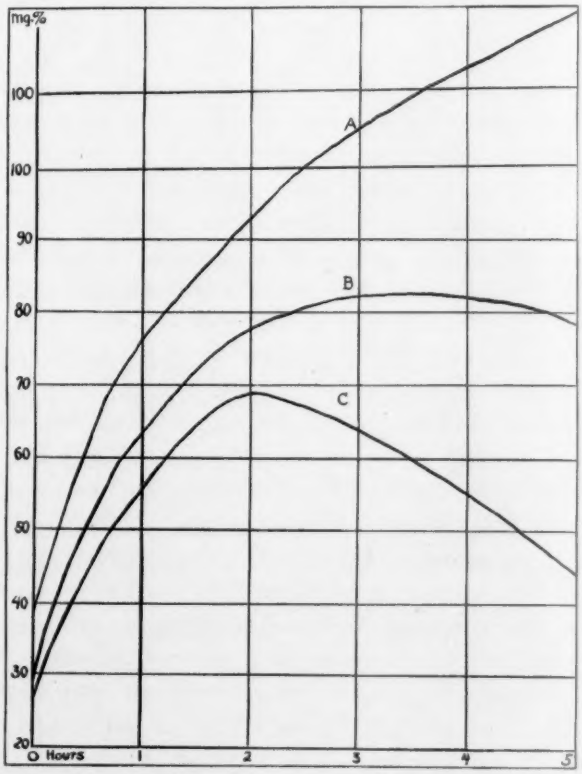

Chart 3.—The concentration of nonfermentable reducing substance in the blood in corrosive mercuric chloride poisoning (*A*), scarlet fever nephritis (*B*) and a normal infant after the ingestion of xylose (*C*).

from accidental mercury poisoning and an infant suffering from scarlet fever with nephritis.

In cases of diabetes, the metabolism of the xylose does not deviate from the normal. In the urine a yeast fermentation must be used to destroy the dextrose. We have had no opportunity to use this reaction in children showing pentosuria.

SUMMARY

A renal function test based on the oral administration of xylose is described. The normal kidney concentrates to over 2.5 per cent of xylose in the urine on the ingestion of 1 Gm. per 3 pounds of body weight, and the xylose is practically removed from the blood stream within five hours. The functionally deficient kidney concentrates less xylose and retains it for a much longer period in the blood. The kidney function may thus be estimated in the blood of infants when the collection of urine is very difficult.

DIPHTHERIA AND DIPHTHERIA CARRIERS IN HOSPITALS FOR THE CARE OF CHILDREN

INCIDENCE, CONTROL AND DETERMINATION OF VIRULENCE; SIGNIFICANCE OF ROUTINE ADMISSION CULTURES

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AND
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The control of diphtheria in any institution for the care of children might center itself around a careful consideration of these points:

1. The chronicity of illnesses such as heart disease, orthopedic conditions, choreas, empyemas and burns, which prolong the period of hospitalization and increase the possibilities for contact.

2. The inadvertent admittance of patients with diphtheria, perhaps indistinguishable at times or even masked by the clinical pictures of colds in the head, follicular tonsillitis or laryngitis.

3. The carriers of diphtheria bacilli, consisting of those recognized by the hospital laboratory and that unrecognized circulating group invariably present among the patients and personnel of such institutions.

4. The lack of alertness among the members of the active unit of the hospital in the use of their knowledge of asepsis in the care of children.

5. The dependence of resting the diagnosis of diphtheria exclusively on reports from the laboratory. A negative report on a culture usually, but not always, excludes a diphtheritic condition.

6. The transfer of patients from one section of the hospital to another for purposes other than isolation for contagious diseases. Occasionally one of these children may harbor diphtheria bacilli.

7. The value of the accepted standard of dismissal of carriers from quarantine. The usual requirement of two or more consecutive negative cultures for termination of the isolation period undoubtedly is of substantial service in limiting the spread of diphtheria. Not infrequently such patients, after being transferred, are found to be harboring the organisms on subsequent cultures. Certainly every one has at times suspected that perhaps common usage rather than the efficiency index of this procedure was responsible for its existence. Often it has seemed to be more of an amusing formality than a useful thumb rule for the limitation of the spread of diphtheria bacilli. It would seem that a false

From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute Laboratory.

sense of security with respect to the dissemination of pathogenic bacteria might be fostered through such arbitrary terminations of the periods of carriers.

The primary purpose of the following study, suggested by Dr. Joseph Brennemann, was the evaluation of nose and throat cultures taken as a routine before and after the admission of patients into the hospital. The questionable interpretation of results, as well as the considerable loss of both time and money, seemed to figure in the practicability of requiring such examinations. Offsetting, perhaps, the value of being forewarned of the presence or absence of diphtheria bacilli, were the possible shortcomings of the procedure, as outlined in the foregoing paragraphs, which actually incited this detailed study.

It is of interest in this connection to know what seems to be the practice of representative hospitals of this country and Canada with respect to the management of the problem of diphtheria in hospitals partially or exclusively devoted to the care of children. Table 1 gives the results of an investigation of 31 hospitals. From this table it would appear that 84 per cent require routine diphtheria cultures on admission, and that 23 per cent have discontinued them; that only 51 per cent of these hospitals make virulence tests on carriers and that 60 per cent make Schick tests on such patients. Sixty per cent of the hospitals apparently quarantine those of their personnel who are found to be carriers, whereas 99 per cent isolate carriers discovered among ward patients.

The Children's Memorial Hospital, virtually a charitable institution, with a capacity of 265 beds, utilizes about 77 per cent of its beds and hospitalizes annually over 4,300 patients. The turnover of the acutely ill outnumbers the chronic patients more than 3 to 1. During the period of this investigation (1929 to 1930), its outpatient department averaged over 12,000 new patients a year, totaling over 46,000 annual visits from sections over most of the city. Since then the visits to the dispensary have increased at least 50 per cent. There are usually 55 graduate nurses, 10 interns and 3 resident physicians who constitute the permanent staff of the hospital. The School of Pediatric Nursing enrolls for instruction during each quarter over 50 student nurses from 12 affiliated hospitals, Their previous training in the practical management of contagious diseases may be regarded as a negligible quantity. Only patients with contagious diseases inadvertently admitted or patients in the institution in whom such diseases have developed are cared for in an isolation section of the hospital composed of 26 beds, partially divided into cubicles or wards with 2 or 4 beds. All patients on admittance have, as a rule, had nose and throat cultures taken, and are assigned to wards of their floors for observation over short variable periods as a precaution against the spread of contagious diseases.

THE METHODS OF STUDY

Routine nose and throat cultures were taken on patients on admittance and occasionally on patients in the dispensary or hospital who had conditions suggesting the possibility of diphtheria.

TABLE 1.—*Information Obtained on the Hospital Control of Diphtheria from Representative Hospitals of the United States and Canada*

Hospital Number	A. M. A. Rating and Beds	N. & T. Cultures: Required on Admission: Private Room	N. & T. Cultures: Required on Admission: Ward	N. & T. Cultures: Discontinued Before Admission	Carriers: Isolated	Carriers: Negative Cultures Required Before Discharge	Virulence Test Made	Contacts Quarantined: Nurses	Contacts Quarantined: Interns	Contacts Quarantined: Employee	Schick Tests Made on: Admissions	Schick Tests Made on: Carriers	Negative Schick Required on: Nurses	Negative Schick Required on: Interns
1	170*	Yes	Yes	No	Yes	...	Yes	Yes	No	No	No	No	Yes	No
2	2,046†	....	No	Yes	Yes	...	Yes	Yes	Yes	Yes	Yes	Yes	No	No
3	80†	Yes	Yes	No	Yes	3	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
4	150†	No	Yes	No	Yes	...	Yes	No	No	No	Yes	No	Yes	No
5	974†	No	No	....	Yes	1-3	No	No	No	No	No	No	No	No
6	200†	Yes	No	No	Yes	3-5	No	Yes	No	Occ.	Yes	Yes	Yes	Yes
7	75†	Yes	Yes	Transfer diphtheria			....	No	....	....	Yes	No		
8	143†	Yes	Yes	No	Yes	3	Yes	No	Yes	Yes	Yes	No		
9	374†	No	Yes	Yes	Yes	2-3	Yes	No	Ward	Yes	Yes	Yes		
10	110†	Yes	Yes	No	Yes	3	No	Yes	Yes	Yes	Yes	No		
11	70	No	No	Yes	No	...	No	No	No	No	No	....		
12	165†	No	Yes	No	Yes	3	No	N&E	No	No	Yes	No		
13	150†	Yes	Yes	No	Transfer diphtheria		....	Yes	....	....	No	No		
14	120†	....	Yes	No	Yes	3	Yes	Yes	Yes	Yes	Yes	....		
15	200*	Yes	Yes	No	Yes	3	Yes	Nurses	No	Yes	Yes	No		
16	166†	Yes	Yes	Yes	Yes	2	Yes	Yes	No	Yes	Yes	Yes		
17	117†	No	No	Yes	Transfer diphtheria		....	Yes	....	....	Yes	No		
18	190*	Yes	Yes	Yes	Yes	3	No	No	Yes	Yes	Yes	No		
19	75†	Yes	Yes	No	Yes	3	No	No	No	Yes	Yes	Yes		
20	747†	Yes	....	....	Yes	3	Yes	No	No	Yes	No	No		
21	150†	Yes	Yes	....	Yes	2	Yes	Yes	No	Yes	No	No		
22	256†	Yes	Yes	No	Yes	2	No	Yes	No	Yes	Yes	Yes		
23	954†	Yes	Yes	....	Yes	3	....	Yes	Yes	Yes	Yes	No		
24	3,300†	....	Yes	No	Yes	3	No	Yes	No	....	Yes	No		
25	240†	Yes	Yes	No	Yes	3	Yes	No	No	No	No	No		
26	75†	....	Yes	....	Yes	2	Yes	Yes	No	No	Yes	No		
27	60	....	Yes	....	Yes	5	No	No	No	No	Yes	No		
28	1,710†	....	Yes	No	Yes	3	No	Yes	No	Yes	No	No		
29	204*	Yes	Yes	Yes	Yes	2	Yes	N&I	No	Yes	No	No		
30	267†	No	Yes	No	Yes	3	No	....	Yes	Yes	Yes	No		
31	1,360†	....	Yes	No	Yes	2-3	No	Yes	No	Yes	No	No		
Totals	Yes.....	17	26	7	30		14	19	8	19	21	6		
	No.....	7	4	18	1		13	11	20	8	10	23		
	?.....	7	1	6	..		4	1	3	4	..	2		

* Approved for internship.
† Approved for internship and resident physicians.

All "positive" Löffler cultures from the general hospital laboratory were checked and subcultured on blood agar for isolation and further identification by fermentation reactions and guinea-pig virulence readings. The results of these virulence tests were correlated with the electrophoretic determinations for pathogenicity as described by Falk and others.[1]

1. (*a*) Falk, I. S.; White, J. L., and Jensen, L. B.: Electrical Determination of Virulence on Diphtheria Cultures, Am. J. Pub. Health **2**:714 (July) 1927. (*b*) Falk, I. S.; Jensen, L. B., and Mills, J. H.: Electrophoresis of Diphtheria Bacilli; Development of Simplified Technique for Electrophoretic Measurement of Virulence of Diphtheria Bacilli, J. Bact. **15**:421 (June) 1928. (*c*) Jensen, L. B., and Falk, I. S.: Electrophoresis of Diphtheria Bacilli, J. Bact. **15**:367 (June) 1928.

A critical analysis was made of "positive" and "negative" cultures obtained by the general hospital laboratory, from 8,282 hospital and dispensary patients, and of another group of 1,008 additional cultures taken in the dispensary by us, from children before tonsillectomy, as these children were to serve as a control group. The contact relations of children with "positive" cultures to other patients or to members of their families were investigated through examinations of hospital, dispensary and social service records, and through visits to the home or through the city health department's reports of contagion.

Bacteriologic Technic.—All initial nose and throat cultures were made on Löffler's medium, supplied to us in the "pillboxes" used by the City Health Department of Chicago. After incubation for eighteen hours at 37 C., smears were made and examined for diphtheria bacilli, Stoltenberg's [2] malachite green stain being used. All cultures reported by the laboratory as "positive" were restreaked on sheep's blood agar and reexamined after from twenty-four to forty-eight hours' incubation. Salt-free broth, described by Falk and his associates, was inoculated with 2 or more isolated colonies for use in both the electrophoresis and the guinea-pig tests for virulence. Subcutaneous injections of 2.5 cc. of the broth cultures were made into each of 2 guinea-pigs, weighing about 250 Gm., 1 of which was protected with 500 units of diphtheria antitoxin. Control tests were discontinued later in the work because necropsy observations were always constant in our animals into which injections of virulent bacilli were made.

Electrophoretic determinations were made by the simplified technic recommended by Falk [1b] in his slide cell method. Each electrophoretic reading consisted of 10 determinations on each slide preparation. At the beginning of the work individual instruction in the use of the method was obtained by one of the authors (M.) from Dr. Falk.

The double strength veal infusion broth of O'Kell [3] and Baxter was used in the fermentation tests to differentiate B. diphtheriae, B. hoffmanni and B. xerosis. The cultures used for the fermentation tests were purified by the pour plate method, in which at least 2 deep, well isolated colonies were picked. These reactions were read after incubations of one, five, ten and twenty-one days.

Over a consecutive period of twenty and one-half months prior to the year 1931, there were approximately 8,282 patients from the hospital and dispensary whose nose and throat cultures were examined for diphtheria bacilli by the general hospital laboratory. Of this group, 407, or 4.9 per cent, were reported "positive" for diphtheria bacilli. From these, 251 were isolated on blood agar; of these, 166, or 61.1 per cent, were virulent, and 85, or 33.9 per cent, were avirulent. Only a single reference was found in the current literature pertinent to the prevalence of positive diphtheria cultures in hospitals for children. Potshinkoff [4] reported 639, or 14.5 per cent, of the cultures positive for B. diphtheriae from

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2. Stoltenberg: Neue Farblosung für Diphtheriebazillen, besonders für Kornchenfärbung, Deutsche med. Wchnschr. **52**:1304 (July 30) 1926. Owen, H. H., and Band, M.: Stoltenberg Differential Stain for Diphtheria, Am. J. Pub. Health **20**:426 (April) 1930.

3. O'Kell, C. C., and Baxter, M.: Fermentation Reactions of the Diphtheria Bacillus, J. Path. & Bact. **27**:439 (Oct.) 1924.

4. Potshinkoff, N. A.: Diphtheria Carriers in Children's Hospitals, Gig. i. epidemiol. **8**:55 (Oct.) 1929.

4,394 children, together with 95 adults in the Vasileostrovsky Children's Hospital in Moscow. The number of cultures of diphtheria bacilli isolated on subculture and those virulent for animals were not recorded by this author.

Cultures from another series of 1,008 pretonsillectomy children were made by us as a control group in this study. The children were not acutely ill. This group was examined over a period of ten months, i. e., from January to October, 1930, inclusive. Cultures "positive" for diphtheria were obtained from 52 patients, or 5.15 per cent. Subcultures of these gave 35, or 67.3 per cent, positive for B. diphtheriae. Of this group of 35 cultures, 21, or 63.6 per cent, were virulent, and 14, or 36.3 per cent, were avirulent. Therefore, among the children to be hospitalized immediately and those entering the dispensary for physical examination prior to the removal of their tonsils, the percentages of incidence of "positive" cultures and the number virulent practically balanced each other, confirming the reliability of these findings. Furthermore, the fact that these figures agree so closely suggests that the general hospital laboratory and we functioned with a comparable degree of efficiency in the examination of cultures for diphtheria bacilli.

Eggleton,[5] of England, found that during periods of nondiphtheritic prevalence, when virulence tests are made from "positive" cultures obtained from school children, that about one-third are virulent and two-thirds are avirulent. He concludes that in the absence of clinical diphtheria such virulent carriers are practically not a source of danger. Again Forbes,[5] another English investigator, discovered that Eggleton's virulence ratio was directly reversed when epidemics are existent, i. e., two thirds of the cultures positive for diphtheria organisms are virulent as compared to one third during nonepidemic periods. In our work, over a period when the number of cases of diphtheria was not above that of the average yearly incidence and when the total number of patients with "positive" cultures inadvertently admitted were separated from cases presumed to have developed within the hospital, it was found that of those admitted about one third, and of those that had developed, nearly two thirds, were virulent. It seems, therefore, that those "positive" cultures developing within institutions have an incidence of virulence comparable to that of extramural epidemics. This reversal, again, of the virulence ratio found by us may be of some theoretical interest or practical value to the examining physician who is obliged to pass on patients admitted whose cultures are positive for diphtheria bacilli, provided, of course, that his decision is modified by the previous history relative to the disease.

The series of 407 "positive" cultures was composed of two large groups: 223 from the hospital and 174 from the outpatient department. Of these 407 cultures, 251 were isolated on subcultures, 123 from the hospital and 128 from the dispensary.

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5. Eggleton, cited by Forbes, J. G.: The Problem of Diphtheria Carrier in London Children of School Age, Pub. Health **36**:323, 1923.

In the hospital group of 123 cultures positive for diphtheria bacilli, 83 contained virulent and 40 avirulent organisms. For study, this large group of 223 "positive" cultures was subdivided into two classes (table 5): those that were "negative" on admission but which developed into "positive" cultures after hospitalization and those that were "positive" on admission into the hospital. The group was composed of 192 carriers and 31 clinical cases of diphtheria. The organisms from all but 4 of the patients with a condition diagnosed as clinical diphtheria were virulent. Sixty-three carriers and 22 cases of clinical diphtheria developed within the hospital, listed as 9 tonsillar and 13 nasal cases of diphtheria, with a mortality rate of 14 per cent. There were inadvertently admitted 138 carriers and 9 patients with clinical diphtheria, the latter recorded as 1 patient with laryngeal, 4 with tonsillar and 4 with nasal diphtheria, with an unknown mortality rate, because these patients were not followed up

TABLE 2.—*Correlation of Morphology, Fermentation Reactions and Virulence of Two Hundred Subcultures of Diphtheria Bacilli*

	(Morphology (Löffler's Medium)							
	Typical				Atypical			
	B. Diphtheriae Fermentation	B. Xerosis Fermentation	B. Hoffmanni Fermentation	Total Fermentation	B. Diphtheriae Fermentation	B. Xerosis Fermentation	B. Hoffmanni Fermentation	Total Fermentation
Number tested.....	160	9	2	171	4	12	13	29
Guinea-pig { Virulent...	...	7*	0	134	2	0	1*	3
Virulence { Avirulent.	...	2	2	37	2	12	12	26

* Discrepancies between sugar reactions and virulence tests of bacilli isolated.

after their transfer to the hospitals for contagious diseases of the city. The high mortality rate within the hospital was due to the fact that diphtheria was always a complication of other diseases of serious character. From the 192 carriers, diphtheria bacilli were isolated in 92 cultures, containing 57, or 62.1 per cent, virulent and 35, or 37.9 per cent, avirulent organisms.

The "positive" cultures derived from the other group of 174 children in the outpatient department yielded 128 subcultures of diphtheria bacilli, of which 75 per cent were virulent. These came from patients whose clinical condition led the physician to suspect diphtheria. None of this group was hospitalized; some were transferred to hospitals for contagious diseases, and others to their homes. The group was composed of 12 patients with nasal and 38 with tonsillar diphtheria; 78 were carriers. Perhaps some of these cases of carriers should have been classified as cases of nasal diphtheria, because only those in which the patient had received antitoxin or in which notes of a membrane had been recorded on the dispensary charts could be listed under that diagnosis in

this statistical analysis. The borderline between a carrier and a patient with nasal diphtheria not infrequently offers difficulties in diagnosis for the clinician; conservatism, or avoidance of stating an opinion in this matter seems to be the trend in practice. A serosanguineous nasal discharge with or without excoriations of the skin, irrespective of a true or pseudomembrane, often raises a serious question as to whether the patient is just a purveyor of the organisms or has the disease.

Of the 200 cultures reported in table 2 as "positive" for B. diphtheriae, 171 were typical and 29 were atypical on the basis of morphology. But 160 of the 171 typical, as well as 4 of the 29 atypical, organisms were identified as true diphtheria bacilli by their fermentation reactions on dextrose and saccharose; the remaining 11 cases of typical and the 25 cases of atypical diphtheria bacilli fell into the diphtheroid class. In 8 instances, indicated in the table by an asterisk, there is an apparent discrepancy between virulence and fermentation reactions, which may have been due to organisms being picked from mixed cultures, since virulence tests were not made again after these bacilli were isolated for fermentation reactions.

Of these 200 cultures reported as "positive" by the general laboratory, 29 were thus adjudged by the authors as atypical diphtheria bacilli. The 25 cultures that were identified as diphtheroids by their fermentation reactions were therefore incorrectly diagnosed, making an error on the safe side of 12.5 per cent. It may be assumed, on the basis of morphologic findings, checked by the fermentation reactions, that 1 of 8 of these cultures reported as positive for diphtheria by the general laboratory was probably negative, with the result that that number of patients were isolated or quarantined, thereby increasing the possibility of contact with other patients harboring virulent diphtheria bacilli. It is problematic, of course, as to which side one should take in respect to the making of such an error, because the reporting of questionable smears as positive for diphtheria bacilli may have been of value in limiting the spread of the disease. For instance, 2 of the 29 typical cultures diagnosed by the same laboratory were confirmed to be true virulent diphtheria bacilli. This means that if these 29 atypical cultures had been diagnosed as negative for diphtheria, only 1 per cent of the entire 200 cultures would have escaped recognition.

The cost of patients maintained in the isolation section of the hospital over a period of one year because they were either carriers or had clinical diphtheria, based on per capita cost, amounted to $24,358.62. If we may assume that in 1 of 8 cases cultures were incorrectly diagnosed "positive," then 21 children were isolated during that period at an expense of $3,049.32, indicating that each error in general costs $145.00. The other losses are: the patient's unnecessary isolation and chance con-

traction of diphtheria or other diseases, such as "crossed-infections," and the moral obligations liable to be incurred by the hospital as a result of having made these so-called conscientious errors, which are immeasurable but deserve thoughtful consideration.

In studying the virulence of our series of diphtheria cultures it was decided to make use of the recent electrophoresis method of Falk and others [1] in connection with the guinea-pig technic. These authors reported that there is a direct correlation between the virulence of the organisms and the rate at which they travel in an electrical field; the electrophoretic mobility of the organisms virulent for the guinea-pig

TABLE 3.—*Thirty Selected Electrophoresis Readings Tabulated with Results of Fermentation and Guinea-Pig Virulence Tests*

Culture	Microns, Second Volts, Cm.	Guinea-Pig Virulence Test	Fermentation of Dextrose	Fermentation of Saccharose	Source
284	2.010	+	+	—	N. diphtheria
283	2.031	+	+	—	Carrier
468	2.041	+	+	—	N. diphtheria
290	2.051	+	+	—	N. diphtheria
388	2.067	+	+	—	Carrier
266	2.269	+	+	—	Carrier
470	2.274	—	—	—	Carrier
286	2.274	+	+	—	L. diphtheria
111	2.451	+	—	—	Carrier
469	2.466	+	+	—	Carrier
317	3.365	+	+	—	N. diphtheria
220	3.651	+	+	—	N. diphtheria
77	3.661	+	+	—	Carrier
20	3.661	—	+	—	Carrier
304	3.661	+	+	—	N. diphtheria
265	3.665	+	+	—	N. diphtheria
130	3.674	—	+	—	Carrier
113	3.684	—	+	—	Carrier
385	3.686	+	+	—	T. and L. diphtheria
144	3.694	+	+	—	Carrier
141	4.712	+	+	—	Carrier
39	4.734	+	0	0	Carrier
7	4.445	+	+	—	Carrier
373	4.755	+	+	—	Carrier
49	4.757	+	0	0	Carrier
191	4.778	—	+	+	Carrier
390	4.778	—	+	+	Carrier
6	2.790	+	+	—	Carrier
180	4.790	+	+	+	Carrier
331	4.792	—	+	+	Carrier

was reported by them to be lower than that recorded for avirulent strains.

The technic used by us for making the electrophoretic determinations and those on guinea-pigs was that described by the investigators mentioned. Electrophoretic readings were made on bacilli obtained from 253 of our cultures. Table 3 shows 30 representative readings of this series for cultures virulent by the guinea-pig method. These ranged from 2.01 to 5.65.

Jensen and Falk,[1c] on 49 electrophoretic determinations on cultures selected from "clinical cases, carriers or suspected cases," gave a range

of from 12.1 to 1.1. In their report their average strains, as identified by sugar reactions and as proved avirulent for the guinea-pig, gave a range in readings from 12.1 to 4.2, whereas their 30 virulent strains, likewise verified by the same tests, gave a range of readings from 4.2 to 1.0.

In our series, it is seen (table 3) that the readings for either the virulent or the avirulent organisms were neither consistently high nor low. That fact did not permit us to separate the readings of these cultures into two groups in order to make this test of any practical value in the determination of the pathogenicity of diphtheria bacilli.

Similarly, Jones,[6] in a recent publication, reported in a study of 34 virulent and several avirulent diphtheria cultures that had previously given characteristic morphologic and fermentation reactions with carbohydrates that virulence or a lack of virulence of organisms for the guinea-pig was not correlated by the observed velocity of electrophoretic migration, because at least 27 of his virulent strains of diphtheria bacilli showed widely divergent rates.

During this period of twenty and one-half months, there was a total of 223 "positive" cultures within the hospital, of which 83 were virulent. Forty-five of the cultures containing pathogenic bacilli developed, presumably, within the hospital. Regardless of the number of positive diphtheria cultures that developed on the floors, only a single case of diphtheria was traceable to direct contact with another patient who had had tonsillar diphtheria. If a positive culture developed in the patient within a month or less from the date of development of the positive cultures found in others on the same floor, he was rated a contact. Even with this liberal allowance of time, only 4 such contacts on as many floors were recorded as possibly traceable to patients "positive" on admittance, as revealed by an investigation of the records. No patients with "positive" cultures were found as contacts to former patients transferred from the isolation pavilion of the hospital whose cultures were "positive" occasionally. However, 17 carriers and 1 patient with nasal diphtheria were considered as possible contacts to other patients whose cultures had been "positive" for diphtheria. These patients had remained on those floors a number of days before their transfer to the isolation section of the hospital.

Of the 407 patients with cultures "positive" for diphtheria, 192 were investigated relative to their probable contact relation to other members of their families, in an attempt to determine whether their positive culture reports could be traced to previous contacts or whether diphtheria had been disseminated by them when they were discharged from the

6. Jones, L.: Virulence and Electrophoresis of Bacillus Diphtheriae, Proc. Soc. Exper. Biol. & Med. **28**:883 (June) 1931.

hospital. This was accomplished in 140 instances, by studying the hospital, dispensary or social service records, through home visits by a coached graduate nurse and through the examination of the city health department's reports of contagion. One or two, or occasionally all, of these sources of information were utilized before our inquiry was complete.

From 71 of 107 carriers and from 7 of the 9 patients with clinical diphtheria inadvertently admitted to the hospital and later discharged after having had 2 consecutive "negative" cultures, only a single carrier

TABLE 4.—*Distribution of Patients in the Hospital, Including Those Who Had Clinical Diphtheria or Harbored B. Diphtheriae or Diphtheroids Over a Period of Twenty and One-Half Months*

	Ward and Beds	Average Days per Patient in Ward	Average Monthly Admittance of Patients	Total Number of Patients in Ward	Admitted with Positive Culture: Ratio of Positive Cultures to Number of Patients in Ward, per Cent		Admitted with Positive Culture: Carriers	Admitted with Positive Culture: Cl. Diph. T.	Admitted with Positive Culture: Cl. Diph. N.	Negative on Admission But Developed Positive Culture Later: Ratio of Positive Cultures to Number of Patients in Ward, per Cent		Negative on Admission But Developed Positive Culture Later: Carriers	Negative on Admission But Developed Positive Culture Later: Cl. Diph. T.	Negative on Admission But Developed Positive Culture Later: Cl. Diph. N.
Patients Hospitalized for Acute Conditions														
	CS–29	9.5	34.5	1,055	1:27	3.4	37	0	2	1:132	0.76	7	0	1
	B–32	9.9	47.6	1,359	1:26	4.2	51	5*	1	1:151	0.66	6	0	3
	C–41	10.7	42.5	1,363	1:65	1.6	21	0	0	1:194	0.51	4	1	2
	D–45	7.8	36.4	1,286	1:18	0.54	7	0	0	1:257	0.38	4	1	0
Totals	147	37.9	161.0	5,063	1:136	9.74	116	5	3	1:734	2.31	21	2	6
Patients Hospitalized for Chronic Conditions														
	E–26	23.1	4.7	408	1:20	0.5	2	0	0	1:20	4.9	16	3	1
	F–31	25.0	10.4	585	1:29	0.34	2	0	0	1:48	2.0	9	1	2
	G–35	22.9	7.3	569	1:42	0.7	4	0	0	1:47	2.1	7	2	3
Totals	92	71.0	22.4	1,562	1:91	1.24	8	0	0	1:153	9.0	32	6	6

CS, infants under 18 months of age; B, floor for acute medical conditions; C and D, medical and surgical floors; F, orthopedic floor; E, convalescent wards; G, cardiac, nephritic and choreic patients.

* Includes 1 case of laryngeal diphtheria.

of diphtheria was found to have developed in the home. However, histories of the patients *prior* to their hospitalization gave the information that 2 cases of diphtheria and 3 carriers had been present in their families. In this group of 5 persons the health department found only 2 "positive" cultures, and organisms from these were avirulent.

It was also possible to trace and investigate the families of 44 of 55 carriers and of 14 of the 22 patients with clinical diphtheria that had developed within the hospital. No history of diphtheria or "positive" cultures was found in the families receiving these discharged patients. The virulence ratio in this group was twice that found in the series mentioned. It appears that the hospital's requirement of but two consecutive "negative" cultures prior to the discharge of the patient has been reasonably satisfactory.

In the distribution of patients within the hospital, as recorded in table 4, the ratio of the wards for acute and chronic conditions in the yearly turnover was about 3 to 1, and 8 to 1 in respect to the average monthly admittance. The length of time that the patient with the chronic condition remained in the hospital was nearly twice that of the acutely ill child. Nearly 10 per cent of the patients entering the hospital for acute conditions had "positive" cultures, and cultures "positive" for diphtheria bacilli developed later in only 2.3 per cent of them. Whereas, in the wards for chronic conditions less than 2 per cent of the patients had "positive" cultures on admission, in 9 per cent of them "positive" cultures developed later. These results seem to indicate that much more importance should be attached to those "positive" cultures developing among children already hospitalized than among those having "positive" cultures on admission. The incidence of "positive" cultures developing in the section of the hospital devoted to chronic patients was nearly four times that found in the section for acute diseases.

It was also observed that at least 30 per cent more cases of clinical diphtheria developed in the wards for patients with chronic conditions than occurred in the wards for the acutely ill.

The admission to the hospital of patients with clinical diphtheria was probably of minor consideration per se in the dissemination of the disease, because of the temporary isolation of all those admitted and the immediate transfer of such patients on diagnosis to the isolation pavilion of the hospital.

In only one or two instances was it possible to suspect that transfers from the quarantine section of the hospital were the source of other patients' developing cultures positive for diphtheria bacilli. Before such patients are ready to be transferred back to their respective wards, 3 consecutive cultures negative for diphtheria are required.

It was not possible to determine or even to estimate the possibilities of acquiring the disease from contacts of patients with adults necessarily in the wards. These adults included, of course, the personnel of the hospital and visitors.

It is seen from table 5 that in the total number of "positive" cultures obtained from admissions 27 per cent were virulent and 16 per cent were avirulent as compared to the group developing among the patients hospitalized, in which more than 50 per cent were virulent and 20 per cent avirulent. However, of the total number isolated on subcultures of both groups, 62 per cent of the former (admitted) and 72 per cent of the latter (developing) contained virulent organisms. In the cultures found to be "positive" on admission, 40 per cent were not isolated on subcultures as compared to 16 per cent in the group developing within the hospital. Of course, there is the probability that a higher percent-

age of diphtheria bacilli would have been isolated had special cultural mediums been employed, but the results obtained by ordinary methods were desirable in our attempt to be practical in this investigation.

Approximately, a total of 508 patients was segregated on "K" for miscellaneous conditions of contagious character (table 4), and in 12, or 2.36 per cent, of the patients "positive" cultures, presumably charged as "crossed infections," developed. Of the 12, however, only 3, or 25 per cent, were found to be virulent, showing on the basis of pathogenicity that this percentage was greatly reduced. For practical purposes, it might be permissible to ignore the 3 cultures in the nonisolated column and assume for conservatism that the culture under the last column

TABLE 5.—*An Analysis of All Cultures* "Positive" for B. Diphtheriae in the Hospital Over the Period of 20.5 Months*

	Positive Cultures from Patients on Their Admission				Cultures from Patients Negative on Admission But Positive Later				
Ward	Number	V.	A.	N. I.	N. E.	Number	V.	A.	N. I.	N. E.
B	57	19	10	21	7	9	4	3	2	0
C	21	6	3	8	4	7	4	2	1	0
D	7	3	0	4	0	5	3	0	0	2
E	2	0	1	0	1	20	13	3	3	1
F	2	1	0	1	0	12	11	0	1	0
G	4	0	1	3	0	12	5	3	2	2
CS	39	5	7	18	9	8	2	1	2	3
K†	6	4	1	0	1	12	3	5	3	1
Total	138	38	23	55	22	85	45	17	14	9

V, indicates virulent; A, avirulent; N. I., failed to isolate B. diphtheriae on subculture; N. E., never examined by authors.

* Include cases of clinical diphtheria; †, isolation section of hospital for contagious diseases; the cultures "positive" under K include only those admitted to it from the outpatient department as presenting emergency cases.

(N.E.) was virulent; then the percentage figure for "crossed infections" for diphtheria bacilli would approximate 0.79 per cent.

In this study, efforts were not made to determine the greatest incidence of cultures positive for diphtheria bacilli in the hospital by systematic, periodic, reculturing, but solely on data received in the routine management of patients. Consequently, if the group under the column of those not isolated had been periodically recultured, doubtless diphtheria bacilli would have been found in a certain percentage of those cultures. A considerable number of cultures of this group (N.I.) were considered by both the general laboratory and the authors as atypical in form in the smears made from the growth on Löffler's medium.

SUMMARY

1. Of 8,282 patients from the hospital and dispensary, there were 407 or about 5 per cent who yielded cultures "positive" for diphtheria

bacilli in the routine examinations made by the general hospital laboratory. From these (407) cultures it was possible to isolate 251 on subcultures, of which 66 per cent were virulent and 34 per cent avirulent. About one half of these came from the hospital; the remainder were derived from the dispensary. There was a somewhat higher percentage (75 per cent) of the cases with virulent organisms found in the cultures taken from the throats of dispensary patients who were not hospitalized in whom clinical diphtheria was suspected.

2. In another control series of 1,008 children who were examined by the authors themselves, in the outpatient department prior to tonsillectomy, 5 per cent yielded cultures "positive" for B. diphtheriae. These patients were examined over a period of ten months, i. e., from January to October, 1930, inclusive. In this group 64 per cent of the cultures were virulent and 36 per cent avirulent.

3. Examination of patients in the hospital showed that approximately 33 per cent of all cultures found to be "positive" on admission were virulent, whereas nearly 66 per cent of the "positive" cultures were virulent that were obtained from hospitalized patients whose cultures were "negative" on admission but who later were suspected of being carriers or of having diphtheria.

4. On the basis of morphology and identification by fermentation reactions, 1 of 8 cultures of a group reported "positive" by the general laboratory was negative for B. diphtheriae, signifying that approximately 12 per cent of these patients harbored diphtheroids and were needlessly isolated. This conservatism or each error in diagnosis represented a cost to the hospital of $145.

5. If all the atypical organisms had been diagnosed as "negative" by the general hospital laboratory, only 1 per cent of the bacilli that proved to be virulent would have been incorrectly diagnosed.

6. In our work, the electrophoresis test as a measure of pathogenicity of diphtheria bacilli was found to be of no practical value.

7. Of 92 carriers and 22 cases of clinical diphtheria in the hospital, less than 0.5 per cent were traceable as direct contacts with persons having had "positive" cultures or clinical diphtheria.

8. Home investigations were made in 73 per cent of the cases in which the patients had had "positive" cultures relative to the probable relation to other members of their families with respect to the dissemination of the disease.

(*a*) In 93, or 67 per cent, of the 138 homes from which the hospital received its patients with records of "positive" cultures on admission, follow-up investigation revealed but 2 previous cases of clinical diph-

theria and 3 carriers. In this group of 5 persons the health department had found only 2 "positive" cultures, and organisms from these were avirulent.

(*b*) No diphtheria or cultures positive for diphtheria bacilli were found to have developed in any of 68 families investigated which had received discharged patients in whom, according to records, "positive" cultures or the disease had developed within the hospital. This would seem to indicate that the requirement of but 2 consecutive cultures negative for diphtheria bacilli prior to the discharge of such patients from the hospital has been reasonably satisfactory.

9. The length of time the patients remained in the wards is apparently one of the most significant factors for the development of either carriers or diphtheria. For instance, nearly 10 per cent of the patients entering the hospital for acute conditions had "positive" cultures, and in 2.3 per cent of them cultures "positive" for diphtheria bacilli developed later; whereas, less than 2 per cent of the patients hospitalized for chronic conditions had "positive" cultures on admission, in 9 per cent "positive" cultures developed later.

The incidence of "positive" cultures developing in the section of the hospital devoted to chronic diseases was nearly four times that found in the other section containing acutely ill patients. These results seem to indicate that much more importance should be attached to the "positive" cultures developing among children already hospitalized than to those obtained on admission.

10. Of the cultures taken on admission "positive" for diphtheria bacilli, only 20 per cent of those isolated were virulent. Therefore only 1 of 5 of these were important from the standpoint of the possibility of spreading the disease.

CONCLUSIONS

Since (*a*) Forty per cent of the "positive" diphtheria cultures taken as a routine did not grow on subcultures and were from a practical standpoint negative for B. diphtheriae, and

(*b*) Only one third of the same cultures from which bacilli were isolated were found to be virulent, making

(*c*) Only 1 of 5 "positive" cultures taken on admission of practical importance from the point of view of disseminating the disease, and

(*d*) On the basis of morphology and fermentation reactions, 12 per cent of the cultures of the group of patients reported as "positive" by the general laboratory harbored diphtheroids and were needlessly isolated at a cost of $145 per patient:

It would seem practical to abolish the routine taking of cultures on admission of patients and to make local clinical conditions the sole criterion for culturing for diphtheria.

ADDENDUM

During the past sixteen months, the routine taking of nose and throat cultures of patients entering the hospital for removal of tonsils has been discontinued. There have been 2,009 tonsillectomies performed over that period. Practically 100 per cent of the children report back to the outpatient department for postoperative examinations within a week from the date of their discharge from the hospital. It was found that about 1 per cent (0.8 per cent) of these had records of "positive" cultures ranging from sixteen to forty-four days prior to their hospitalization. Also, it may be assumed that 5 per cent of the children of this series of 2,009 patients had "positive" cultures, as did the 1,008 that were examined under similar conditions for the authors' control group.

A sedulous search of the dispensary and social service records of these 2,009 patients revealed no information that diphtheria had been present in these families either before or following the hospitalization of the group studied.

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ACID-BASE BALANCE OF NEW-BORN INFANTS

III. INFLUENCE OF COW'S MILK ON THE ACID-BASE BALANCE OF THE BLOOD OF NEW-BORN INFANTS

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Study of the acid-base balance of normal new-born infants has revealed interesting variations from the standards established for adults.[1] It has been shown that the acid-base balance of the blood is definitely affected during the short period of partial dehydration and starvation which infants undergo the first few days of life. From the data at present available, it is impossible to say whether there is some underlying abnormality in the acid-base metabolism of the new-born infant or whether adults, subjected to similar dehydration and starvation, would manifest an equivalent change in the blood. Direct comparison of the changes induced by dehydration in infants and adults is fallacious since adults practically never lose 8 per cent of their body weight in the course of two or three days as do infants, except in the presence of persistent vomiting or other causes which directly influence the acid-base balance of the blood. Mere deprivation of food and water never produces the same effect on the body weight of adults.

There are other extraneous factors which may influence the acid-base balance of the blood and which are more amenable to a comparative study. One of these factors is the inorganic composition of ingested food. Diets which yield either acid or base ashes affect the acid-base metabolism of the body since they are capable of changing the reaction of the urine.[2] However, physiologic regulation by the normal kidney is sufficient to compensate for any alterations in the acid-base ratio of the intake so that such changes are not reflected in the blood of adults.[3]

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1. (*a*) Hoag, Lynne A., and Kiser, William H., Jr.: Acid-Base Equilibrium of New-Born Infants: I. Normal Standards, Am. J. Dis. Child. **41**:1054 (May) 1931. (*b*) Marples, Eleanor, and Lippard, Vernon W.: Acid-Base Balance of New-Born Infants: II. A Consideration of the Low Alkaline Reserve of Normal New-Born Infants, Am. J. Dis. Child. **44**:31 (July) 1932.

2. Blatherwick, N. F.: The Specific Rôle of Foods in Relation to the Composition of the Urine, Arch. Int. Med. **14**:409 (Sept.) 1914

3. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, p. 965.

Comparatively little work has been done on the response of infants to changes in acid-base intake. Schloss and Harrington [4] reported that the addition of potato gruel to a milk diet caused a diminution of the bicarbonate of the blood of infants due perhaps to the acid ash of potatoes. György, Kappes and Kruse [5] found that in infants who were receiving cow's milk there was a lower carbon dioxide content of the serum than in those who were breast fed. They felt that this was due, in part, to the greater proportion of inorganic acid ions in cow's milk.

In continuation of these studies on normal new-born infants, we have, therefore, thought it desirable to investigate further the response of these subjects to the relatively slight alterations in the acid-base intake that occur when the feeding is changed from human to cow's milk.

MATERIAL AND METHODS

The infants chosen for this study were patients in the obstetrical nurseries of the New York Nursery and Child's Hospital who were found on examination to be normal in every respect. The selection was similar to that of previous groups in this series.[1] Those who had any increase in temperature, clinical evidence of dehydration, vomiting or unusual weight loss were excluded.

The average birth weight for the entire series of sixty-seven infants was 3,229 Gm. (7 pounds and 2 ounces), varying between 2,268 Gm. (5 pounds) and 4,592 Gm. (10 pounds and 2 ounces). No effort was made to differentiate between values found in males and females, as they have been found to be approximately equal.[1a]

The first group comprised forty-five infants who, because of failure to gain satisfactorily on breast feeding after the initial weight loss, were offered cow's milk formulas. In twenty-five cases, breast feeding was discontinued, and a dilution of cow's milk was substituted. In twenty other cases, nursing was complemented with a similar formula. Only those who accepted at least 1 ounce (28 Gm.) of formula after each nursing were included. Because of the similarity in the results obtained, these forty-five infants are hereafter considered as one group. Specimens of blood were taken for analysis after the infants had received formulas for an average of five days.

The effect of alterations in diet may be more clearly seen when the acid-base status of the blood is studied in the same infant both before

4. Schloss, O. M., and Harrington, H.: Comparison of the Carbon Dioxide Tension of the Alveolar Air and of the Hydrogen-Ion Concentration of the Urine with the Bicarbonate of the Blood Plasma, Am. J. Dis. Child. **17**:85 (Feb.) 1919.

5. György, P.; Kappes, F., and Kruse, F.: Das Säure-Basengleichgewicht im Blut, mit besonderer Berücksichtigung des Kindesalters. I. H-Ionenkonzentration und CO_2-Gehalt, Ztschr. f. Kinderh. **41**:700, 1926.

and after the change. A second group of twenty-two new-born infants was studied in this manner. They were breast fed until they had partially regained their initial loss in weight, at which time breast feeding was abruptly discontinued and a cow's milk formula substituted. The first specimen of blood for analysis was obtained immediately prior to this alteration in feeding, which took place at an average age of 5.2 days. Second analyses of the blood were made after the infants had been fed entirely on dilutions of cow's milk for either three or four days. With two exceptions, there was a gain in weight during this interval averaging 97 Gm. (3 ounces).

The routine feedings in both groups consisted of dilutions of two-thirds cow's milk and one-third water with approximately 5 per cent added carbohydrate in the form of cane sugar.

Specimens of blood for analysis were obtained at the same time of day and from two and one-half to three hours after the last feeding. In all infants, crying was either induced or spontaneous during the collection of blood. The blood was obtained by puncture of the external or internal jugular vein and immediately immersed under paraffin oil. The methods employed were the same as for previous work in this series.[1b] All analyses were made on serum.

RESULTS

Study of the acid-base balance of the blood in the first group of forty-five infants was limited to determinations of p_H, carbon dioxide and chlorine. These analyses were made after the infants had been receiving cow's milk either entirely (table 1, part 1) or in addition to breast milk (table 1, part 2) for at least two days. For purposes of comparison, table 2 was constructed using the average figures for this group of infants receiving cow's milk and for a similar group of breast-fed new-born infants previously reported.[1b] It may be seen that the only difference between these two groups was a decrease in the average carbon dioxide content of the serum when cow's milk was fed.[6] These results confirmed the report of György, Kappes and Kruse.[5] The averages for p_H and chloride for the two series were essentially the same.

The range encompassing isolated analyses of the blood of new-born infants is very wide, so that the actual effect of the dietary change is more significant when observed in the same infant. The twenty-two infants thus studied have been assembled to form group 2 of this series, and the detailed data are presented in table 3. The analyses include

6. The table gives the means and their probable errors. When the difference between the means is three or more times the difference of the probable errors, it is considered to be significant.

TABLE 1 (Part 1).—*p_H CO_2 and Cl in the Serum of Twenty-Five New-Born Infants Receiving Cow's Milk*

Case	Birth Weight, Gm.	Weight When Blood Was Studied, Gm.	Age When Formula Was Started, Days	Age When Blood Was Studied, Days	Serum p_H	Serum CO_2 Content		Serum NaCl	
						Per Cent by Volume	mM.	Mg. per 100 Cc.	mM.
1	3,288	3,317	5	16	7.40	52.3	22.2	601	102.8
2	3,033	2,949	10	18	7.41	51.1	21.7	591	101.1
3	2,892	3,033	4	15	7.43	48.0	20.5	582	99.5
4	3,771	3,402	10	23	7.33	47.8	20.2	597	102.1
5	3,033	3,005	6	9	7.42	46.4	19.8	620	106.0
6	3,573	3,402	5	17	7.33	53.3	22.5	578	98.8
7	2,693	2,466	7	10	7.40	41.9	17.8	649	111.1
8	2,830	2,863	5	8	7.38	48.3	20.5	602	102.9
9	3,345	3,118	5	19	7.32	43.6	18.4	582	99.6
10	3,911	3,573	6	9	7.47	51.0	21.8	604	103.3
11	2,438	2,182	6	11	7.43	53.1	22.6	665	113.8
12	2,830	3,033	7	9	7.47	47.0	20.1	611	104.5
13	2,353	2,210	5	9	....	51.6	22.2	606	103.7
14	3,573	3,288	6	8	7.42	43.5	18.5	639	109.4
15	2,977	2,977	3	6	7.34	54.5	23.0	644	110.2
16	3,752	3,629	7	12	7.47	49.8	21.3	600	102.6
17	2,579	2,523	1	4	....	56.1	24.1	580	99.2
18	4,592	4,393	1	3	7.49	53.2	22.8	604	103.4
19	4,082	4,082	9	12	7.37	49.6	21.1	627	107.2
20	3,146	2,949	4	10	7.32	38.6	16.3	628	107.5
21	2,664	2,325	1	3	7.40	46.6	19.8	...	.....
22	2,664	2,296	1	6	7.38	46.0	19.5	653	111.6
23	2,830	2,693	7	10	7.44	37.9	16.1	615	105.2
24	2,268	2,210	3	7	7.39	46.1	19.6	628	107.5
25	3,430	3,288	3	7	7.39	43.6	18.5	625	106.8
Aver.	3,142	3,008	5	10	7.40	46.8	20.4	614	105.0

TABLE 1 (Part 2).—*p_H CO_2 and Cl in the Serum of Twenty New-Born Infants Receiving Complementary Formulas of Cow's Milk in Addition to Breast Milk*

30	3,062	3,062	2	6	7.48	51.2	21.9	643	110.1
31	2,551	2,438	2	7	7.40	47.9	20.4	617	105.5
32	2,892	2,892	2	5	7.35	50.8	21.5	599	102.6
33	3,118	3,118	2	7	7.42	51.1	21.8	605	103.4
34	2,830	2,830	8	11	7.42	53.1	22.6	615	105.2
35	3,175	3,146	8	10	7.36	44.0	18.6	614	105.0
36	2,608	2,410	7	11	7.40	44.1	18.7	644	110.2
37	3,969	3,969	4	8	7.30	49.3	20.7	601	102.8
38	2,664	2,722	6	8	7.30	49.3	20.7	612	104.7
39	2,807	2,579	7	10	7.51	42.4	18.2	624	106.6
40	3,463	3,373	6	10	7.44	50.2	21.4	589	100.7
41	2,977	2,722	7	10	7.43	46.8	20.0	587	100.3
42	2,693	2,608	1	6	7.41	41.8	17.8	636	108.9
43	2,778	2,636	1	6	7.38	35.5	15.1	645	110.3
44	4,167	3,855	3	7	7.37	34.0	14.4	621	106.2
45	2,892	2,579	5	9	7.42	49.4	21.0	646	110.5
46	3,232	2,892	5	7	7.33	57.0	24.0	632	108.1
47	4,307	3,997	15	19	7.39	44.6	18.9	625	106.8
48	2,920	2,920	7	10	7.37	53.0	22.5	624	106.7
49	3,496	3,260	4	7	7.38	53.4	22.7	686	117.4
Aver.	3,130	3,000	5	9	7.39	47.4	20.1	623	106.6
Av. for parts 1 and 2	3,167	3,005	5	10	7.40	47.1	20.3	618	105.7

protein and total base in addition to p_H, carbon dioxide and chlorine. The first analyses of the blood were made while the infants were receiving breast milk and the second analyses three or four days after the shift to cow's milk. This change from breast milk to cow's milk caused a decrease in p_H, carbon dioxide and total determined acid (sum of bicarbonate, chlorine and protein) of the blood. The average figures for chloride and total base were the same for the two types of food.

There was also a decrease in protein in this group of twenty-two infants, but this may be considered normal for the range of ages studied. The average protein content of the serum of the previously reported normal breast-fed infants [1b] at 5 days of age was 6.26 per cent, and at 8 and 9 days, 5.96 per cent, a decrease of 0.30 per cent as

TABLE 2.—*Statistical Evaluation of the Constants Derived from the Data Presented in Table 1*

		Mean	Probable Error	Difference Between Means	Difference of Probable Errors	Difference / Difference Probable Error
p_H	Breast milk	7.40111	0.00434	0.00437	0.00896	...
	Cow's milk	7.39674	0.00785			
CO_2, per cent by volume	Breast milk	52.06500	0.49666	4.29167	0.72434	5.9
	Cow's milk	47.77333	0.52726			
Bicarbonate, mM	Breast milk	22.14500	0.21418	1.83833	0.31080	5.9
	Cow's milk	20.30667	0.22523			
NaCl, mg. per 100 cc.	Breast milk	625.28205	2.40745	7.16842	3.42386	2.1
	Cow's milk	618.11363	2.43455			
Chloride, mM	Breast milk	106.95895	0.69106	1.22621	0.81043	1.5
	Cow's milk	105.73274	0.42336			

compared with a decrease of 0.24 per cent in this series. On the other hand, there was a tendency for the carbon dioxide to increase during this age period, the average for breast-fed infants at 8 and 9 days being 1 per cent by volume higher than at 5 days. In normal breast-fed infants, there was no change in the sum of bicarbonate, chloride and protein during this age period.

A study of table 3 indicates that there is a change in the carbon dioxide content of the blood following a shift to cow's milk. In sixteen of the twenty-two infants studied the carbon dioxide in the blood increased. In some instances, this change was marked, while in others it was barely significant. Of the other six cases, two (127 and 136) showed a very slight increase. The maximum increase was noted in case 134 in which the carbon dioxide rose from 37.4 to 50.5 per cent by volume. From the high figure for serum protein (7.12 per cent) it may be surmised that this infant was in a state of mild dehydration at the time when the first analysis of the blood was made, and that during

TABLE 3.—*Acid-Base Balance of the Serum of Twenty-Two Normal New-Born Infants* *

Case	Birth Weight, Gm.	Age, Days	Weight, Gm.	p_H	CO_2 Content: Per Cent by Vol.	CO_2 Content: mM.	p Co_2, Mm.	Chloride: NaCl, Mg. per 100 Cc.	Chloride: mM.	Protein: Per Cent	Protein: mM.	Phosphate, Sulphate and Total Acid, mM.	Organic Acids, mM.	Total Base, mM.
121	3,997	1	3,940	7.40	51.2	21.8	36.4	601	102.7	5.91	15.0	139.5	8.6	148.1
		4	3,657	7.29	41.6	17.4	37.5	624	106.7	6.55	15.8	139.9	13.4	153.3
124	3,288	7	2,920	7.42	57.4	24.4	39.0	672	114.9	6.14	15.7	155.0	6.3	161.3
		11	3,317	7.42	55.1	23.5	37.5	639	109.3	5.37	13.7	146.5	9.0	155.5
125	3,203	5	2,750	7.33	49.9	21.2	35.5	632	109.0	6.50	16.4	146.6	13.8	160.4
		9	3,005	7.41	56.4	24.0	39.2	580	99.3	5.51	14.0	137.3	12.9	150.2
126	3,402	5	3,175	7.37	60.9	25.9	43.3	643	109.9	5.62	14.2	150.0	....	147.8
		8	3,260	7.38	64.9	27.5	48.1	615	105.3	5.29	13.3	146.1	2.4	148.5
127	3,232	6	3,033	7.43	60.6	25.9	40.3	592	101.3	6.71	17.2	144.4	0.7	145.1
		9	3,203	7.41	63.0	26.8	43.7	613	104.9	5.95	15.1	146.8	9.8	156.6
128	3,543	6	3,496	7.42	57.4	24.5	39.1	648	110.9	5.64	14.4	149.8	....	143.4
		9	3,571	7.25	43.1	18.0	42.3	634	108.3	5.50	13.0	139.3	13.8	153.1
129	3,373	6	3,203	7.42	56.8	24.2	38.6	616	105.4	5.47	14.0	143.6	1.0	144.6
		10	3,402	7.31	39.3	16.5	34.0	649	111.0	5.96	14.5	142.0	1.8	143.8
130	3,430	5	3,232	7.42	51.7	22.0	35.2	624	106.7	5.79	14.8	143.5	3.2	146.7
		9	3,430	7.41	47.7	20.3	33.2	634	108.5	5.82	14.8	143.6	11.0	154.6
131	3,573	6	3,601	7.43	60.9	25.9	41.4	633	108.3	5.23	12.8	147.0	....	144.4
		9	3,629	7.42	51.8	22.1	35.2	628	107.4	6.00	15.3	144.8	7.3	152.1
132	3,430	6	3,373	7.42	50.2	21.4	34.1	651	111.3	5.30	13.5	146.2	12.7	158.9
		10	3,260	7.33	41.6	17.5	34.1	645	110.4	5.55	13.6	141.5	9.1	150.6
133	3,317	5	3,203	7.42	59.0	25.1	40.1	640	109.4	5.50	14.0	148.5	9.6	158.1
		8	3,317	7.38	51.4	21.8	38.1	633	108.2	5.43	13.6	143.6	7.8	151.4
134	3,515	6	3,260	7.30	37.4	15.7	33.0	629	107.6	7.12	17.2	140.5	13.5	154.0
		9	3,373	7.33	50.5	21.3	41.5	623	106.6	6.25	15.3	143.2	8.3	151.5
135	3,855	6	3,685	7.43	55.1	23.5	36.7	620	106.0	6.96	17.8	147.3	11.1	158.4
		9	3,883	7.44	50.9	21.7	33.1	640	109.5	6.11	15.7	146.9	0.3	147.2
136	2,949	4	2,835	7.38	55.9	23.7	41.5	616	105.4	5.86	14.7	143.8	3.8	147.6
		7	2,920	7.38	58.1	24.7	43.1	618	105.6	5.79	14.4	144.7	4.8	149.5
137	3,883	4	3,855	....	54.8	23.3	38.9	575	98.3	7.01	17.7	139.3	3.9	143.2
		7	3,911	7.36	50.5	21.4	39.2	640	109.4	5.59	13.9	144.7	9.6	154.3
138	3,175	5	3,033	7.41	58.2	24.8	40.5	658	112.5	5.60	14.2	151.5	2.2	153.7
		8	3,118	7.34	55.9	23.6	45.2	629	107.6	5.61	13.8	145.0	8.2	153.2
139	2,807	7	2,722	7.39	57.9	24.6	42.0	634	108.5	5.96	15.0	148.1	4.3	152.4
		11	2,778	7.39	34.7	14.7	25.2	669	114.5	6.02	15.2	144.4	8.3	152.7
140	3,232	6	2,920	7.37	54.4	23.0	41.2	677	115.9	6.45	16.1	155.0	3.6	158.6
		9	3,090	7.40	63.6	27.1	45.2	638	109.2	5.71	14.4	150.7	6.7	157.4
141	3,430	4	3,203	7.42	52.2	22.2	35.5	598	102.2	6.16	15.7	140.1	12.3	152.4
		7	3,232	7.34	47.5	20.0	38.4	647	110.7	5.66	14.0	144.7	10.5	155.2
142	3,855	4	3,571	7.42	56.6	24.1	38.5	630	107.7	5.42	13.8	145.6	8.0	153.6
		8	3,685	7.41	52.6	22.4	36.6	641	109.7	5.59	14.2	146.3	10.3	156.6
143	3,062	6	2,977	7.37	60.8	25.8	46.1	626	107.0	5.71	14.3	147.1	4.5	151.6
		9	2,962	7.41	55.2	23.5	38.4	609	104.2	5.51	14.0	141.7	7.9	149.6
144	3,628	4	3,288	7.41	62.0	26.4	43.1	636	108.8	5.19	13.2	148.4	9.8	158.2
		7	3,317	7.34	42.8	18.1	34.6	643	109.9	5.35	13.2	141.2	14.1	155.3
Av. on breast milk	3,417	5.2	3,240	7.40	55.5	23.6	39.1	630	107.7	5.97	15.1	146.4	5.5	151.9
Av. on cow's milk		8.5	3,333	7.37	50.8	21.4	38.3	631	108.0	5.73	14.3	143.7	8.7	152.4

* In each instance, the first analysis was made while the infant was receiving breast milk and the second after the substitution of cow's milk.

the three days when he received cow's milk he recovered sufficiently to reach the average figure for infants on this type of food. No explanation can be offered for the failure of the carbon dioxide to decrease in the remaining three cases (125, 126 and 140). However, statistical analysis (table 4) indicated that the average figures for the whole group of twenty-two showed a definitely lower carbon dioxide content of the serum after cow's milk had been substituted for breast milk.

From table 4, it may be seen that the changes in p_H, carbon dioxide, protein and total acid were significant. Since the changes in chloride

TABLE 4.—*Statistical Evaluation of the Constants Derived from the Data Presented in Table 3*

		Mean	Probable Error	Difference Between Means	Difference of Probable Errors	Difference / Difference Probable Error
p_H	Breast milk	7.39857	0.00514	0.02812	0.00878	3.2
	Cow's milk	7.37045	0.00712			
CO_2, per cent by volume	Breast milk	55.51364	0.78324	4.68637	1.40066	3.3
	Cow's milk	50.82727	1.16121			
Bicarbonate, mM	Breast milk	23.60909	0.33876	2.20454	0.70350	3.1
	Cow's milk	21.40455	0.61657			
NaCl, mg. per 100 cc.	Breast milk	629.59091	3.54077	1.81818	4.37629	...
	Cow's milk	631.40909	2.57194			
Chloride, mM	Breast milk	107.71364	0.60882	0.29545	0.75044	...
	Cow's milk	108.00909	0.43876			
Protein, per cent	Breast milk	5.96591	0.08519	0.23318	0.09684	2.4
	Cow's milk	5.73273	0.04607			
Base bound by protein, mM	Breast milk	15.07727	0.21135	0.76818	0.24238	3.2
	Cow's milk	14.30909	0.11866			
Total acid, mM.*	Breast milk	146.40000	0.57834	2.54091	0.72088	3.5
	Cow's milk	143.85909	0.43034			
Total base, mM	Breast milk	151.93182	0.86878	0.44091	0.99506	...
	Cow's milk	152.37273	0.45516			

* Total acid represents the sum of bicarbonate, chloride and protein.

and total base were statistically insignificant, it became apparent that the balance of the acid-base system was maintained by an increase in some unanalyzed acid. In this group fall phosphates, sulphates and organic acids. It is unusual to find an accumulation of organic acids in the blood. The amount present in food is usually small and is oxidized in the body except during carbohydrate starvation. The carbohydrate intake of infants receiving cow's milk with added cane sugar was sufficient so that if there was actually an increase in organic acids of the blood, one must presuppose an inadequate utilization of the carbohydrate, a point for which there is at present no confirmatory evidence. The amounts of phosphate and sulphate ions normally present in the serum are small (3 mM. HPO_4'' and 1.0 mM SO_4''), and significant increases

occur only in the presence of marked renal insufficiency. The greater inorganic phosphorus content of cow's milk may be responsible for an increase of phosphorus in the serum, but our data furnish no conclusions on this point.

In view of the wide range of individual figures for isolated analyses of the blood of new-born infants, it was considered desirable to determine the daily variation in individual breast-fed infants. Seven normal new-born infants were selected for this purpose, and analyses were made on three or four successive days. Table 5 gives the results for this

TABLE 5.—*Acid-Base Balance of the Serum of Normal Breast-Fed Infants (Controls) on Successive Days*

Case	Birth Weight, Gm.	Age, Days	Weight, Gm.	p_H	CO_2 Content: Per Cent by Vol.	CO_2 Content: $p\,CO_2$, mM.	CO_2 Content: $p\,CO_2$, Mm.	Chloride: NaCl, Mg. per 100 Cc.	Chloride: mM.	Protein: Per Cent	Protein: mM.	Phosphate, Sulphate and Total Acid, mM.	Organic Acids, mM.	Total Base, mM.
A	3,657	7	3,780	7.43	48.3	20.6	32.1	682	116.6	5.84	15.0	152.2	3.6	155.8
		8	3,799	7.46	48.6	20.8	30.2	656	112.3	5.79	15.0	148.1	....	.....
		9	3,855	7.33	47.3	19.9	38.8	656	112.3	6.31	15.4	147.6	7.4	155.0
		10	3,940	7.36	54.8	23.2	42.5	636	108.8	5.96	14.8	146.8	7.8	154.6
B	3,771	7	3,911	7.41	57.1	24.3	39.7	627	107.3	5.21	13.2	144.8	....	.....
		8	3,925	7.41	58.7	25.0	40.8	...	.....	5.24	13.3	.....	....	152.4
		9	3,855	7.39	65.2	27.7	47.3	616	105.4	5.16	13.0	146.1	....	.....
C	3,232	6	3,146	7.42	64.5	27.5	43.8	604	103.3	5.47	14.0	144.8	12.7	157.5
		7	3,146	7.42	65.4	27.9	44.4	622	106.4	5.35	13.6	147.9	4.3	152.2
		8	3,146	7.42	57.9	24.7	39.3	618	105.7	5.73	14.6	145.0	9.1	154.1
D	3,402	6	3,345	7.35	47.5	20.1	37.9	631	108.0	6.14	15.2	143.3	9.6	152.9
		7	3,373	7.39	53.8	22.8	39.0	654	111.8	5.75	14.5	149.1	8.0	157.1
		8	3,288	7.40	57.5	24.5	40.9	633	108.2	5.36	13.7	146.4	10.7	157.1
E	3,629	5	3,496	7.43	66.2	28.2	44.0	616	105.3	5.46	14.0	147.5	13.7	161.2
		6	3,515	7.43	66.9	28.5	44.5	628	107.4	5.06	13.0	148.9	9.0	157.9
		7	3,515	7.43	66.0	28.1	43.9	626	107.0	4.79	12.3	147.4	14.5	161.9
F	3,288	4	3,345	7.37	56.3	23.8	42.6	646	110.5	5.42	13.5	147.8	12.8	160.6
		5	3,345	7.41	60.5	25.7	42.0	626	107.2	5.40	13.9	146.8	7.8	154.6
		6	3,317	7.40	58.2	24.7	40.4	615	105.2	5.43	13.7	143.6	10.1	153.7
G	2,920	7	3,005	....	48.3	20.5	35.1	610	104.3	6.04	15.3	140.1	14.1	154.2
		8	3,033	7.34	51.1	21.6	41.4	628	107.4	6.06	14.7	143.7	14.7	158.4
		9	3,062	7.42	54.4	23.2	37.0	624	106.7	5.46	13.9	143.8	13.9	157.7

group. It is apparent that there were daily variations in the acid-base status of the blood of breast-fed infants, but the general trend during the age period studied (from 4 to 10 days) was a rise in the carbon dioxide as long as the infants were gaining weight. The consistency of these figures leads to the conclusion that the changes observed when infants were changed to cow's milk were not the result of a normal daily variation.

COMMENT

Many explanations for the decreased alkaline reserve in new-born infants receiving cow's milk have been mentioned (Freudenberg[7] and

7. Freudenberg, E.: Störungen des Säurebasenaushaltes beim Kinde, Klin. Wchnschr. **5**:2049, 1926.

Meyer and Nassua [8]). A brief discussion of their applicability in the light of the more complete analyses of the acid-base balance presented here should be interesting. Any explanation must rest largely on the differences in composition of human and cow's milk since this was the only factor changed in the infants' regimen.

The inorganic constituents of cow's milk exceed those of breast milk. Exact comparison of the inorganic composition of the two kinds of milk is difficult on account of uncontrollable fluctuations in mineral content (Macy and her co-workers [9]). We have arbitrarily selected the figures reported by Holt, Courtney and Fales [10] for the inorganic composition of breast milk during the first twelve days of the lactation period and those of Sherman [11] for cow's milk. These data are given

TABLE 6.—*Inorganic Composition of Human and Cow's Milk*

	Human Milk*			Cow's Milk**	
	Mg. in 100 Gm. Milk	Cc. N/10 in 1,000 Gm. Milk		Mg. in 100 Gm. Milk	Cc. N/10 in 1,000 Gm. Milk
K_2O	93.8	199.2	K	143	365.7
Na_2O	45.3	146.1	Na	51	221.7
CaO	44.6	159.1	Ca	120	599.0
MgO	10.1	50.1	Mg	12	98.7
Total base	....	554.5	.....	...	1,285.1
P_2O_5†	41.0	49.8	P†	93	539.3
Cl	56.8	160.2	Cl	106	298.9
Total acid	....	210.0	.....	...	838.2
Ratio acid:base	....	1:2.6	.....	...	1:1.5

* Data for human milk from: Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**: 229 (Oct.) 1915. The figures represent the average of five analyses of milk obtained within the first twelve days of the infant's life.

** Data for cow's milk from Sherman, Henry C.: The Chemistry of Food and Nutrition, New York, Macmillan Company, 1928.

† In calculating the base-binding power of phosphorus, the valence was considered to be 1.8.

in table 6. It is obvious that the total intake of inorganic elements is much greater when cow's milk is fed. In a dilution of two-thirds cow's milk and one-third water there are 1.5 times as much base and 2.7 times as much acid as in an equal amount of breast milk. From the point of view of acid-base balance, the ratio of acid to base is more

8. Meyer, L. F., and Nassua, E.: Die Säuglingsernährung, Munich, J. F. Bergmann, 1930, p. 34.

9. Macy, I. G.; Nims, B.; Brown, M., and Hunscher, H. A.: Human Milk Studies: VII. Chemical Analysis of Milk Representative of the Entire First and Last Halves of the Nursing Period, Am. J. Dis. Child. **42**:569 (Sept.) 1931.

10. Holt, L. E.; Courtney, A. M., and Fales, H. L.: A Chemical Study of Woman's Milk, Especially Its Inorganic Constituents, Am. J. Dis. Child. **10**:229 (Oct.) 1915.

11. Sherman, Henry C.: Chemistry of Food and Nutrition, New York, The Macmillan Company, 1928.

interesting. In human milk there is one part of acid to 2.6 parts of base as compared to a ratio of 1:1.5 for cow's milk. There is, therefore, a definite change in the acid-base ratio of the intake when cow's milk is fed. We are then confronted with the question as to whether this relatively minor change in the acid-base ratio of the intake is sufficient to produce a decrease in the alkaline reserve of new-born infants.

The effect of slight changes in the acid-base ratio on the alkaline reserve of the blood of adults has been studied by numerous investigators whose results in some instances are conflicting. McClendon and his co-workers [12] found practically no change in the alkaline reserve of the blood after three day experimental periods during which diets with either acid or alkaline ashes were ingested, and concluded that the alkaline reserve of adults is remarkably resistant to the influence of diet. Michalowsky [13] reported that an acid diet (meat, fats, cereals, beans and cocoa) fed to normal adults for from three to five weeks did not cause any diminution of the alkaline reserve of the blood. Tolstoi [14] determined the carbon dioxide content of the blood of two healthy men at monthly intervals throughout a year while on a diet of meat and fat. The carbon dioxide remained within normal limits in spite of the daily ketonuria and in spite of the ingestion of a diet the inorganic composition of which was distinctly acid.

On the other hand, Schwarz and Dibold [15] found a slight increase in the carbon dioxide of the blood the first day after a basic diet of rice and fruit had been started, and this increase was more marked on the second day. The alkaline reserve was diminished when an acid diet of meat was used. Hasselbalch [16] studied the influence of dietary changes on the tension of alveolar air. A vegetable diet was capable of producing significant increases in the carbon dioxide tension, while a meat diet decreased it.

Children are apparently more susceptible to acidosis than adults.[17] Ketosis, with the consequent diminution of the carbon dioxide of the

12. McClendon, J. F.; von Meysenbug, L., Engstrand, O. J., and King, F.: Effect of Diet on the Alkaline Reserve of the Blood, J. Biol. Chem. **38**:539, 1919.

13. Michalowsky, Ernst-Heinrich: Alkalireserve und säure Kost, Klin. Wchnschr. **9**:1505, 1930.

14. Tolstoi, E.: The Effect of an Exclusive Meat Diet on the Chemical Constituents of the Blood, J. Biol. Chem. **83**:753, 1929.

15. Schwarz, H., and Dibold, H.: Diätetische Beeinflussung des Säure-Basenhaushaltes, Deutsche med. Wchnschr. **57**:1324, 1931.

16. Hasselbalch, K. A.: Neutralitätsregulation und Reizbarkeit des Atemzentrums in ihren Wirkungen auf die Kohlensäurespannung des Blutes, Biochem. Ztschr. **46**:403, 1912.

17. Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: II. Ketosis and the Respiratory Exchange in Children, Am. J. Dis. Child. **31**:335 (March) 1926.

blood, may be induced with ease by starvation (Gamble [18]) or by high fat diets (Sawyer and her associates [19]). The effect of alterations of the inorganic constitutents in the food on the acid-base balance of children without the simultaneous production of ketosis apparently has received little attention. Morgan and Hatfield [20] studied the effect of supplementary lunches with ashes of varying composition on the alkaline reserve of children. There was an increase in the carbon dioxide content of the blood at the end of an experimental period of from twenty-eight to fifty days when diets with a basic ash were fed. The maximum change was observed in a child who received a supplementary lunch (dried figs), the ash of which had the highest basic content. These increases in alkaline reserve were accompanied by marked increases in body weight. The effect of mixed and of vegetable diets on the alveolar carbon dioxide tension of malnourished children was studied by Lane and Bosshardt.[21] The alveolar carbon dioxide tension increased as the children gained weight, but there was no marked difference between the two dietary groups. The mixed diet had an acid-base ratio of approximately 1 : 1.3 and the vegetable diet of 1 : 2.3, a difference which is comparable with that between breast and cow's milk.

Studies on animals have shown definite effects on the carbon dioxide of the blood as a result of acid or base ash-forming diets. Page [22] reported such findings in rabbits; Samuel and Kugelmass [23] in rats, and Michalowsky [13] in guinea-pigs.

Data in this paper would indicate that changes in the acid-base equilibrium of the blood were more easily induced in new-born infants than in either adults or children, although it fails to give an insight into the underlying cause. In adults, the kidneys are largely responsible for maintaining the acid-base balance of the blood. The thesis that the kidneys are incapable of maintaining the balance of the blood of new-born infants cannot be proved by the data at present available.

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18. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923.

19. Sawyer, M.; Steyens, F. A., and Baumann, L.: Studies of Acid Production: I. The Varying Susceptibility of Children to Acidosis, Am. J. Dis. Child. **15**:1 (Jan.) 1918.

20. Morgan, A. F., and Hatfield, G. S.: The Effect of Various Supplementary Lunches on the Plasma Carbon Dioxide Capacity of Children, Am. J. Dis. Child. **32**:655 (Nov.) 1926.

21. Lane, D. E., and Bosshardt, F. H.: Nutrition of Children on a Mixed and on a Vegetable Diet, Am. J. Dis. Child. **40**:285 (Aug.) 1930.

22. Page, I. H.: The Effect of Diet on the Alkaline Reserve and Insulin Hypoglycemia in Rabbits, Am. J. Physiol. **66**:1, 1923.

23. Samuel, E. L., and Kugelmass, I. N.: Comparative Studies of the Influence of Acid-Forming and Base-Forming Diets on the Metabolism of Rats, Am. J. Dis. Child. **39**:687 (April) 1930.

Thorough proof would involve careful study of the secretion of urine and of its composition under the influence of varying diets.

A change from breast to cow's milk may involve other factors besides the acid-base ratio of the ingested food. The organic composition of milk must be considered. The substance that is most often held responsible for the decrease in the carbon dioxide content of the serum of infants receiving cow's milk is the protein. Breast milk during the first twelve days of the lactation period, has a protein content ranging from 2.0 to 2.6 per cent (Holt et al.[10]), and whole cow's milk has a protein content of 3.3 per cent (Sherman[11]). However, in the dilutions used in feeding these infants (two-thirds milk and one-third water) the protein content of the mixture is approximately 2.2 per cent and very nearly the same as breast milk.

In considering protein, however, the total content is of far less importance than the types of protein present. According to Meyer and Nassua,[8] the greater casein content of cow's milk may, theoretically, retard digestion and delay emptying of the stomach, but they state further that the experimental evidence on this point is inconclusive.

The retardation of gastric digestion brings up the question of the possible effect of digestive secretion on the acid-base balance of the blood. In order to minimize these influences, all of the samples of blood used in this study were withdrawn at the same time of day and from two and one-half to three hours after the last meal. Changes in the carbon dioxide content of the blood due to secretion of digestive juices are the result of primary changes in chloride or total base.[24] The fact that chloride and total base were the same for infants receiving cow's milk as for infants receiving breast milk would indicate that variations in digestion do not explain the lower carbon dioxide content of the serum in the former group.

In the duodenum and small intestines, the p_H is optimal for the fermentative digestion of proteins of breast milk.[8] The milieu is acid, which permits the reabsorption of organic acids and their further combustion in the body. When cow's milk is fed, the intestinal processes tend to become more alkaline and form fatty acids which are found in the stools combined with calcium to form insoluble soaps.[8] Freudenberg[7] believes that this creates a steady drain of fixed base from the body which, in turn, causes the decrease in the carbon dioxide of the blood. However, the more complete data given in this paper would indicate that there is no such diminution of the fixed base concentration of the blood.

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24. Gamble, J. L., and McIver, M. A.: The Acid-Base Composition of Gastric Secretions, J. Exper. Med. **48**:837, 1928; The Acid-Base Composition of Pancreatic Juice and Bile, ibid., p. 849.

The structure of milk is very complex, and an attempt to trace it through the animal organism involves a study of the entire metabolism. To ascribe the lowering of the carbon dioxide content of the serum to any one or more differences between cow's milk and human milk is impossible with our present knowledge. However, it seems incredible that the mere shift from human to cow's milk should produce a greater change in the acid-base balance of the blood of new-born infants than is produced by more marked dietary fluctuations in adults. That it does, would indicate that the acid-base metabolism of new-born infants is less capable of rapid readjustment to extrinsic factors.

CONCLUSIONS

In new-born infants receiving whole cow's milk there is a slightly lower carbon dioxide content of the serum than in infants receiving breast milk. This diminution in carbon dioxide is accompanied by a decrease in p_H and an increase in unanalyzed acid.

The differences in the composition of human and cow's milk and their contribution to alterations in the acid-base status of the blood have been discussed.

The results indicate a greater lability of the acid-base balance of the blood of new-born infants, but the underlying cause cannot be determined from the data at present available.

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RESOLVING EXUDATES IN PULMONARY TUBERCULOSIS OF CHILDHOOD

STUDY I

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The observation that exudates in a tuberculous lung might completely resolve was apparently first made by French clinicians [1] in the nineteenth century. These reports, though frequently mentioned in the literature, had little influence on the views concerning the pathogenesis of pulmonary tuberculosis. In 1922 Assmann [2] and in 1923 Wessler and Jaches [3] described the infraclavicular infiltration as a typical early form of adult pulmonary tuberculosis. Haudek and Fleischner [4] soon pointed out that these early lesions had remarkable powers of resolution. In the year previous to Assmann's publication Eliasberg and Neuland [5] had reported the complete resolution of lobar exudates in tuberculous children, and Kleinschmidt [6] in 1919 had called attention to the resolution of extensive exudates which he had observed in several children suffering from pulmonary tuberculosis. The first cases in the American literature were published by Gerstenberger and Burhans [7] in 1927 in their report on the use of ultraviolet rays in pulmonary tuberculosis of infants and children. They called attention to the massive lobar distribution of these shadows, as well as to the good prognosis, indicated the difficulty of differentiating the condition in some of the cases from lobar pneumonia and expressed the opinion that the exudates were probably specifically tuberculous.

It was soon realized that the observations made by these and other observers were of crucial importance. Despite an extensive literature,

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From the Babies and Childrens Hospital and the Department of Pediatrics, Western Reserve University.

1. Neumann, W.: Ergebn. d. ges. Tuberk. **2**:259, 1931.

2. Assmann, H.: Ergebn. d. ges. Tuberk. **1**:119, 1930.

3. Wessler, H., and Jaches, L.: Clinical Roentgenology of Diseases of the Chest, Troy, N. Y., The Southworth Company, 1923, p. 69.

4. Haudek, M., and Fleischner, F., quoted by Assmann (footnote 2).

5. Eliasberg, H., and Neuland, W.: Jahrb. f. Kinderh. **93**:88, 1921; **94**:102, 1921.

6. Kleinschmidt, H., in Engel and Pirquet: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, vol. 1, p. 502.

7. Gerstenberger, H. J., and Burhans, C. W.: Treatment of Extensive Pulmonary Tuberculosis with Ultraviolet Rays, Am. J. Dis. Child. **33**:54 (Jan.) 1927.

however, there is still no unanimity concerning the nature of these lesions. This is shown by the fact that there are as many names for the lesions as there are writers on the subject. Some have suggested that the shadows seen in the roentgenogram are caused by atelectases.[8] The pressure of enlarged mediastinal nodes has been thought to be sufficient to produce the collapse. Others believe that these shadows are due to an infection of the respiratory tract by the common pyogenic organisms,[9] and since the clinical frequency of resolving exudates in cases of pulmonary tuberculosis is greater than a merely casual relation would permit, Winckler assumed that tissue infected with the tubercle bacillus is a *locus minoris resistentiae* for other common organisms.[10] Another group [11] denies altogether the inflammatory character of many of these lesions and regards them as areas of edema, perhaps with some increase in connective tissue. Huebschmann [11b] described the microscopic picture of lymphatic congestion which he believes is not uncommonly found in the vicinity of tuberculous processes, particularly when these are accompanied by fibrosis. He expressly stated that the disappearance of such edematous areas might simulate a resolution of a tuberculous exudate. Without questioning the correctness of Huebschmann's observations, I doubt their importance, for, if one carefully excludes all exudates of an inflammatory character, the number of cases of extensive pulmonary edema due to lymphatic congestion is certainly small. Even cases of fibrotic phthisis, in which the obstruction to lymph flow is much greater, show more often a dry tissue than extensive edema. How small must be the obstruction in the childhood type of tuberculosis in which fibrosis plays a comparatively insignificant rôle! I also believe that the extraordinary wealth of collaterals that the lymph system of the lungs possesses has been underestimated.[12] When one recalls to mind the homogeneous dense lobar shadows that are so often seen in tuberculosis in children, it seems quite improbable that they could be produced by lymphatic congestion.

The majority of the workers, however, regard the exudates as inflammations that occur in association with tuberculous tissue but that are not themselves tuberculous and are not caused by the immediate

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8. (a) Duken, J.: Die Besonderheiten der roentgenologischen Thoraxdiagnostik im Kindesalter, Jena, Gustav Fischer, 1924, p. 94. (*b*) Kleinschmidt, H.: Tuberkulose der Kinder, Leipzig, Johann Ambrosius Barth, 1927, p. 91. (*c*) Wallgren, A.: Acta radiol. **7**:595, 1926.

9. Duken (footnote 8*a*, p. 97).

10. Winckler, A., quoted by Duken (footnote 8*a*, p. 97).

11. (*a*) Koch, Walter: Monatschr. f. Kinderh. **29**:303, 1925. (*b*) Huebschmann, P.: Pathologische Anatomie der Tuberkulose, Berlin, Julius Springer, 1928, p. 244.

12. Miller, W. S.: Am. Rev. Tuberc. **3**:193, 1919.

presence of tubercle bacilli.[13] The noxious agent is supposed to be a poison from the destroyed tissue or a "toxin" from the tubercle bacillus in the focus of "true" tuberculous inflammation. This conception is difficult to state in a tangible fashion and has led to the use of a galaxy of terms: perifocal inflammation of a nonspecific nature, collateral inflammation, epituberculosis, circumfocal inflammation, protein body pneumonia, hilar catarrh, paratuberculosis, perituberculous inflammation and congestive pneumonia.[14]

Common to all of these writers is the disinclination to regard a lesion that resolves completely as caused by the direct action of the tubercle bacillus. The literature is cognizant of the possibility that tuberculous pneumonias may escape caseation and undergo a complete *restitutio ad integrum*,[15] but a generation born to a tradition of pessimism in the prognosis of extensive pulmonary tuberculosis, and yet confronted with the clinical facts of recovery, prefers to dispute the specificity of the regressive lesions. Pulmonary tuberculosis like a stubborn foe is retreating tardily from the field. In 1902, Dettweiler [16] could still write that "only a few years ago the diagnosis of pulmonary tuberculosis was regarded as a death warrant whose execution could merely be delayed." Readers of Trudeau's autobiography [17] will recollect the black despair that filled his heart on hearing Janeway's diagnosis of pulmonary tuberculosis. "I think I know something of the feelings of the man at the bar who is told he is to be hanged on a given date, for in those days pulmonary consumption was considered as absolutely fatal." It is of immediate interest for the present discussion that Dettweiler considered the disinclination to diagnose the disease except in terminal cases the cause of this state of mind, "all others being regarded as mere catarrhs."

The universality of the positive tuberculin reaction demonstrated beyond doubt the benign nature of most tuberculous infections. The methods of physical diagnosis, however, could not demonstrate the early stages of the disease, and only advanced cases came to the eyes of the physician. Hence, when the routine use of the roentgenogram revealed the resolving character of many lesions in the course of indubitable pulmonary tuberculous disease, clinicians were inclined to deny their specific nature. Unwittingly they returned to conceptions of an earlier

13. Kleinschmidt (footnote 6). Huebschmann (footnote 11*b*, pp. 99, 222 and and 240).

14. Duken (footnote 8*a*). Koch (footnote 11*a*).

15. Beitzke, H., in Aschoff, L.: Pathologische Anatomie, ed. 5, Jena, Gustav Fischer, 1921, vol. 2, p. 309.

16. Dettweiler, P.: Die Anstaltsbehandlung der Tuberkulose der Atmungswege (edition of G. Besold), Berlin, G. Reimer, 1902, p. 195.

17. Trudeau, E. L.: An Autobiography, New York, Doubleday, Doran & Company, Inc., 1928, p. 71.

era, which taught that much of the inflammation found in tuberculous lungs was merely accessory and incidental to the tuberculous process.

Laennec taught:

> Sometimes I have observed the last mentioned [conglomerate tubercles] in lungs affected with peripneumonia, and even in the hepatized portion. The small number, limited extent and very pale colour of the tuberculous masses made it evident that they were of recent formation, but from this we must most certainly not conclude that the tubercles were the outcome of inflammation, for besides such a case being extremely rare when compared with the frequency of hepatization of the lung, I have also found the same variety of tubercles at the same stage in patients whose lungs were in all other respects perfectly healthy. M. Bayle has moreover proved conclusively that tubercles cannot be regarded as a result of the termination of inflammation.
>
> It cannot, indeed, be denied that peripneumonia, both acute and chronic, is sometimes co-existent with tubercles: it is even probable that it may occasion their development in patients already predisposed; whereas, in other cases, the irritation set up by the presence of tubercles, in appreciable numbers, may determine peripneumonia.
>
> We cannot but give credence to these two possibilities, in view of repeated post-mortem examinations; on the other hand, a multitude of facts shows that the development of tubercles is the outcome of some general condition, that it most often takes place without any previous inflammation, and that when inflammation is coincident with tubercular disease, it is usually of a later date.[18]

To extricate oneself from this confusing situation one must first consider the evidence that the proponents of the views mentioned offer. There is no doubt but that atelectasis is an important factor in the pathology of tuberculosis. This is due, for the most part, to the development of tubercles in the immediate vicinity of the ultimate respiratory radicles; the consequent pressure produces a stenosis and finally a collapse of the passage and thereupon an airlessness of the parts distal to the points of pressure. Another cause of atelectasis is the fibrosis, which may be a prominent part of healing. I have seen a primary infection (Ghon's focus) whose path of lymphatic drainage to the bronchopulmonary lymph nodes was completely airless. In neither of these cases, however, would massive homogeneous roentgenologic shadows result, the characteristic feature of which is the comparative speed of resolution. The only mechanism that could produce this is a pressure by enlarged lymph nodes on the primary bronchi. It is not impossible that very large right paratracheal nodes may by direct pressure compress the right upper lobe in the small dome of a child's thorax. I have seen an autopsy that suggested this mechanism. The importance of atelectasis, however, should not be overestimated. The

18. (*a*) Long, Esmond R.: Selected Readings in Pathology, Springfield, Ill., Charles C. Thomas, 1929, p. 159. (*b*) Fraenkel, A.: Spezielle Pathologie und Therapie der Lungenkrankheiten, Berlin, Urban & Schwarzenberg, 1904, p. 626.

number of autopsies or bronchoscopic observations by which lymphadenopathy has been proved to be the cause of atelectasis is small. The physical and roentgenologic signs by which this condition is usually diagnosed [19]—the decrease in the size of the atelectatic lobe, its retraction toward the hilus and the movement of the diaphragm and mediastinum toward the affected part [20]—are usually not found. Often the shadow occupies a position in the peripheral or median lung fields, e. g., Assmann's infraclavicular infiltration, which could hardly be selectively and exclusively collapsed by any such mechanism. Certain modes of resolution, such as that described by McPhedran [21]—in which the exudate retreats dorsomedially and so tends to produce a wedge-shaped infiltrate in the paravertebral regions—cannot be satisfactorily explained by assuming the reinflation of an atelectatic lung. When one further considers that many of the patients have all the symptoms of a severe infection and that roentgenograms not infrequently show pleural thickenings, it seems most improbable that an inflammatory exudate is absent.

I do not doubt but that some of the resolvable shadows in the course of a pulmonary tuberculosis are simple nontuberculous bronchopneumonias or lobar pneumonias. It is, however, not proper to impose this valid conclusion on the entire subject and to consider resolution as indicative of a nontuberculous, or more specifically, a pyogenic etiology. The more intensive the roentgenologic study of cases of pulmonary tuberculosis is, the more frequently does the clinician find resolving shadows. The frequency, therefore, is greater than one would have the right to expect from a merely casual coexistence of the two diseases, and one would have to conclude that tuberculous tissue—or even normal tissue from an allergic person—is particularly susceptible to infection with pyogenic organisms. This, in fact, is what some authors have suggested.[10] Here again there is an outcropping of a historic error in the study of tuberculosis. Within the span of the present generation authorities taught that the septic fever of phthisis was due to secondary infection; cavita-

19. Bowen, D. R.: Acute Massive Collapse (Atelectasis) of the Lung, Am. J. Roentgenol. **21**:101, 1929. Packard, E. N.: Massive Collapse (Atelectasis) Associated with Pulmonary Tuberculosis and Tumor, Am. Rev. Tuberc. **18**:7, 1928. Stoloff, E. G.: Acute Massive Atelectasis of the Lung Complicating a Fresh Tuberculous Primary Complex, Am. J. Dis. Child. **35**:239 (Feb.) 1928.

20. I have seen a case (J. B.), which will be reported in the AMERICAN JOURNAL OF DISEASES OF CHILDREN in an article entitled "The Use of the Lateral and Oblique Chest Diameters in the Roentgenographic Study of Pulmonary Disease in Childhood," in which an atelectatic right middle lobe had retracted and produced in the roentgenogram a convex shadow at the hilus. Autopsy revealed the condition described: tubercles of the conglomerate type, fibrosis and atelectasis, throughout the entire lobe. Compare this with Epstein's report cited later in this article.

21. McPhedran, F. M.: Am. Rev. Tuberc. **20**:532, 1929.

tion, pus formation and even coagulation necrosis were not caused by the tubercle bacillus but by organisms that secondarily invaded the "weakened" tissue. A quotation from Penzoldt and Stintzing's "Handbuch der Therapie," [22] published in 1902, will fortify this statement:

> Although the tubercle bacillus is the fundamental cause of pulmonary tuberculosis and only requires some support from environment or disposition, it is not the exclusive cause of all the pathology that passes under the name of "pulmonary tuberculosis." Just as other pathogenic bacteria aid the tubercle in invading the tissue, so they aid it later in its work of destruction (mixed infection). Some of the attacks during the course of the disease and the end-stages are perhaps the result of the activity of the streptococci found in sputum (pyogenes, pyocyaneus, tetragenus, etc.), i.e., the result of purulent and septic processes (compare with the newest compilation by Sata). The proposal that those processes called forth chiefly by the tubercle bacillus be named pulmonary tuberculosis whereas those which depend chiefly on the aid of other bacteria be named pulmonary phthisis has much to be said in its favor; however, much speaks against it.[22a]

These views were based on a bacteriologic technic that today must be regarded as inadequate. It is not surprising that smears and cultures from cavities or even from the lung itself should reveal many of the common inhabitants of the respiratory tract. Histologic section, however, does not demonstrate the ubiquity that one would expect from a germ of etiologic significance. Hence a writer who has critically reviewed the subject of secondary infection said:

> Just as in the case of typhoid ulceration, so in tuberculous inflammation, many workers believe that the destruction of tissue is not due to typhoid or tubercle bacilli but to pyogenic organisms which come to the aid of the tubercle bacilli. . . . Bacteriologic examination of the cavity walls has in our experience revealed pyogenic bacteria now and then, but we have never been able to discover any massive penetration of streptococci. . . . According to our observations the action of associating bacteria in complex cases of tuberculosis has been overemphasized. . . . It is indeed remarkable how little nontuberculous disease one finds in autopsy on phthisical patients and how few concomitant infections occur in tuberculous wards.[23]

This relative resistance to secondary infection was also observed by Petroff,[24] who found a greater mortality from acute and chronic pyogenic infections in his control guinea-pigs than in those infected with fatal doses of tubercle bacilli.

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22. Penzoldt and Stintzing: Handbuch der Therapie innerer Krankheiten, Jena, Gustav Fischer, 1902, vol. 3, p. 318.

22a. A criticism of these views was given by Fraenkel (footnote 18*b*, pp. 692 and 699).

23. Pagel, W., and Henke, F., in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1930, vol. 3, pt. 2, p. 139.

24. Petroff, S. A.: Immunity in Tuberculosis, J. A. M. A. **89**:285 (July 23) 1927.

A correct understanding of the pathogenesis of tuberculous exudates is impossible unless one frees oneself from the restrictions of rigid morphologic concepts. The tubercle is too often regarded as exhausting the content of the term specific tuberculous tissue; it is forgotten that no less specific is the exudate, which consists, for the major part, of fluid rich in protein and fibrin, lymphocytes and wandering cells that have gone under various names, such as epithelioid, "exudate" cells, large mononuclears, etc. Not even these characteristic elements need be present in inflammatory exudates of tuberculous origin. Large areas of the lung may be filled with nothing more than fibrin, albuminous fluid and a few nondescript round cells, and yet the tuberculous nature of the inflammatory material is proved by the presence of tubercle bacilli and even of coagulative necrosis.[25] The attempt has even been made to draw the limits of specificity within the narrow radius of the tubercle. The somewhat loose assembly of round cells and albuminous exudate in the wall of the tubercle has been differentiated by some as a nonspecific perifocal inflammation from the denser nucleus to which alone the privilege of specificity has been given.[26] This conception has been utilized to explain the resolving exudate of pulmonary tuberculosis. It has always seemed unreasonable to me that these restrictions should be placed on tuberculous inflammation whereas such niceties are not demanded in describing inflammation of other origin. The staphylococcus abscess has a peripheral zone of inflammation that differs in histologic characteristics from the interior, yet one does not call on any other agencies than the staphylococcus to explain its pathogenesis. From a purely histologic standpoint the "perifocal reaction" of the tubercle does not differ from that of the early tuberculous pneumonia, an opinion that Marchand [27] has expressed and that can easily be verified by a cursory examination of specimens from phthisical lungs.

The versatility of living tissue in its reaction to the tubercle bacillus has been most clearly recognized by experimental research workers. Massive reinfection of a guinea-pig usually produces not the typical mononuclear exudate but a purulent inflammatory response. Exactly the same result follows in man when in pulmonary tuberculosis cavities rupture into the pleural cavity. Pyopneumothorax is the result of infection with tubercle bacilli, as the absence of other organisms shows. Such an exudate—composed largely of polymorphonuclear leukocytes, fibrin and serum—when found in the alveoli may lead the examiner astray, and thus, I believe, many fresh areas of pneumonia in tuber-

25. For classic descriptions of early tuberculous pneumonia see (*a*) Duken (footnote 8*a*, p. 99) and (*b*) Askanazy (in Aschoff: Pathologische Anatomie, ed. 5, Jena, Gustav Fischer, 1921, vol. 1, p. 202).

26. Huebschmann (footnote 11*b*, p. 98).

27. Marchand, F., quoted by Duken (footnote 8*a*, p. 100).

culous lungs are erroneously regarded as products of secondary invaders. Such errors are particularly prone to occur when the patient dies shortly after an eruption of caseous material into the bronchial system. A routine stain [28] for tubercle bacilli would, in my opinion, afford more convincing evidence as to the etiology of these "nonspecific inflammations." Askanazy called attention to this occurrence in Aschoff's "Pathologische Anatomie." [25b]

REPORT OF CASES

At the Babies and Childrens Hospital two cases that illustrate these views have recently been observed.

CASE 1.—J. S., a colored child, aged 3½ years, was infected by the father and died after rapid progress of the disease. Autopsy revealed caseous pneumonia of the upper portions of the right middle lobe and right lower lobe. The latter area was the site of a large cavity. The lower portion of the right lower lobe was extensively infiltrated by many small conglomerate tubercles between which there was consolidated but intact lung tissue. The microscopic picture of this intervening tissue, which is of particular interest for this discussion, will be given with that of case 2.

CASE 2.—J. A. was a white infant of 4 months who had been infected by the mother. On admission to the hospital, the child was suffering from bronchial obstruction of the left main bronchus by a ball-valve mechanism. With the return of the heart and mediastinum to their normal position, an infiltration of the entire left lung developed. This cleared, leaving an area of infiltration in the central lung field which subsequently spread progressively throughout the left lung until the child's death. The clinical diagnosis, which was substantiated by autopsy, was tuberculous mediastino-adenitis and bronchiogenic distribution of caseous material in the left lung. Here again areas of bronchopneumonia were found in the left lower lobe which awakened interest because of their nonspecific morphology. Dr. Alan R. Moritz, of the Institute of Pathology, Western Reserve University, furnished the report on the pathologic changes in these cases (as well as the photomicrographs).

Autopsy.—The lungs in both cases were the seat of extensive tuberculous inflammation, the right being more involved than the left in case 1, and the left more than the right in case 2. The outstanding difference in the type of inflammation seen in the two cases was in the acuity of the process. In case 1 there was almost no reactive tissue change, the process being principally exudative and necrotizing with no tubercle formation. In case 2 there were miliary and conglomerate tubercles in addition to large areas of exudative and necrotizing consolidation. In both cases there was ulcerative tuberculosis of the mucosa of major bronchi.

The pneumonia, which was extensive in both cases, was in places caseous. The exudative cells were principally polymorphonuclear leukocytes with occasional endothelial phagocytes and were intra-alveolar. The character of the exudate varied from place to place, being purulent, seropurulent, fibrinopurulent and hemorrhagic. The interstitial tissue showed no change over large areas, and the blood vessels

28. In this connection it is perhaps well to call attention to the fact that tissue fixed in formaldehyde may give poor or negative results with the acid-fast stain for tubercle bacilli.

were patent, and in places dilated. The bronchi and bronchioles contained the same kind of exudate as seen within the alveoli. The bronchiolar epithelium and the cells lining air sacs were frequently desquamated, but did not manifest unusual degenerative changes. Caseous necrosis was seen in case 2, with and without tubercle formation, while in case 1 it was entirely independent of tubercle formation, and its extension was through the establishment of independent foci rather than by contiguity with a primary necrotic focus.

In the pneumonic areas, large numbers of intra-alveolar acid-fast organisms were present, and although their concentration was greater in necrotic areas,

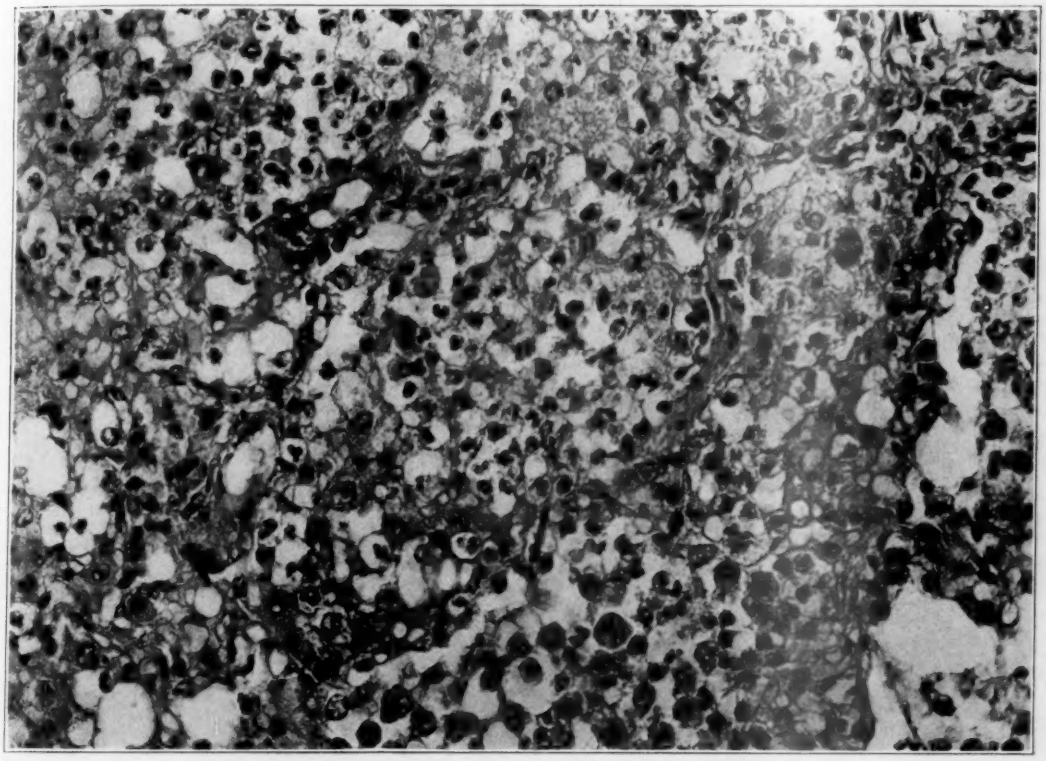

Fig. 1 (case 1).—Tuberculous pneumonia; reduced from a magnification of × 450.

their distribution was general. The organisms varied in size, were often granular and exhibited some tendency to be disposed parallel to one another; although most of them were distributed free in the exudate, occasional intracellular forms were seen.

In both cases there was extensive tuberculous bronchopneumonia. The pneumonia did not represent an inflammation collateral to tubercle formation, but rather an independent process of apparently aerogenous extension. It differed from ordinary bronchopneumonia in the presence of acid-fast organisms and the tendency on the part of the exudate to undergo caseous necrosis with extension to include the pulmonary parenchyma.

SUMMARY

In these two cases not only the classic caseous pneumonia and tubercle but areas of infiltration were observed which grossly were indistinguishable from the commonplace bronchopneumonia of non-tuberculous origin. Microscopically these areas were the site of sero-purulent, fibrinopurulent and hemorrhagic inflammation, yet a Ziehl-Neelsen stain revealed tubercle bacilli in large numbers. From this, one can infer that the simple morphology of an inflammatory exudate does

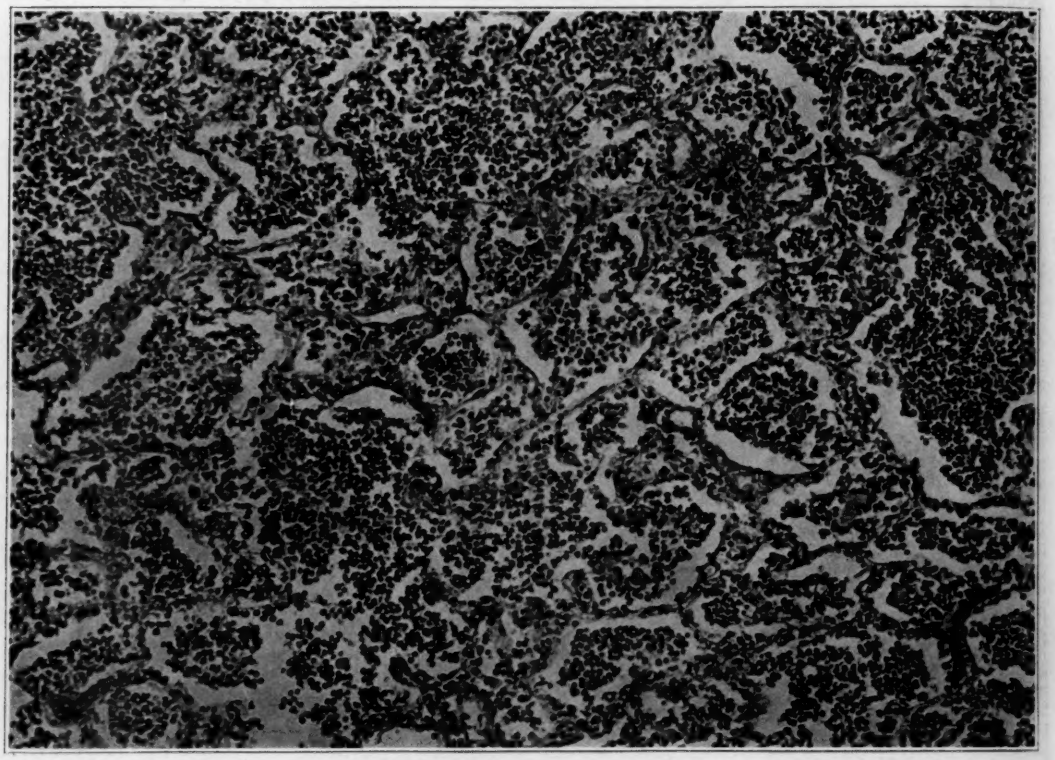

Fig. 2 (case 1).—Tuberculous pneumonia; reduced from a magnification of × 125.

not give sufficient grounds for excluding a tuberculous etiology. If the concept of perifocal inflammation of nonspecific etiology is to be retained, it must be based on tissue stains that exclude the presence of the tubercle bacillus. It should, moreover, by no means be inferred that the type of inflammation described is characteristic of the resolving exudate. Nothing is known of its course. Indeed, there are no reasons for doubting that any form of tuberculous inflammation, short of actual massive caseation, can resolve.

From the clinician's standpoint there would be justification for a differentiation between the tuberculous tissue of characteristic construction and that without this specific architecture, if it could be shown that thereby one would gain knowledge of prognostic significance. However, on the one hand, as has been mentioned, the albuminous exudate that fills such large areas of tuberculous lungs and that is almost entirely

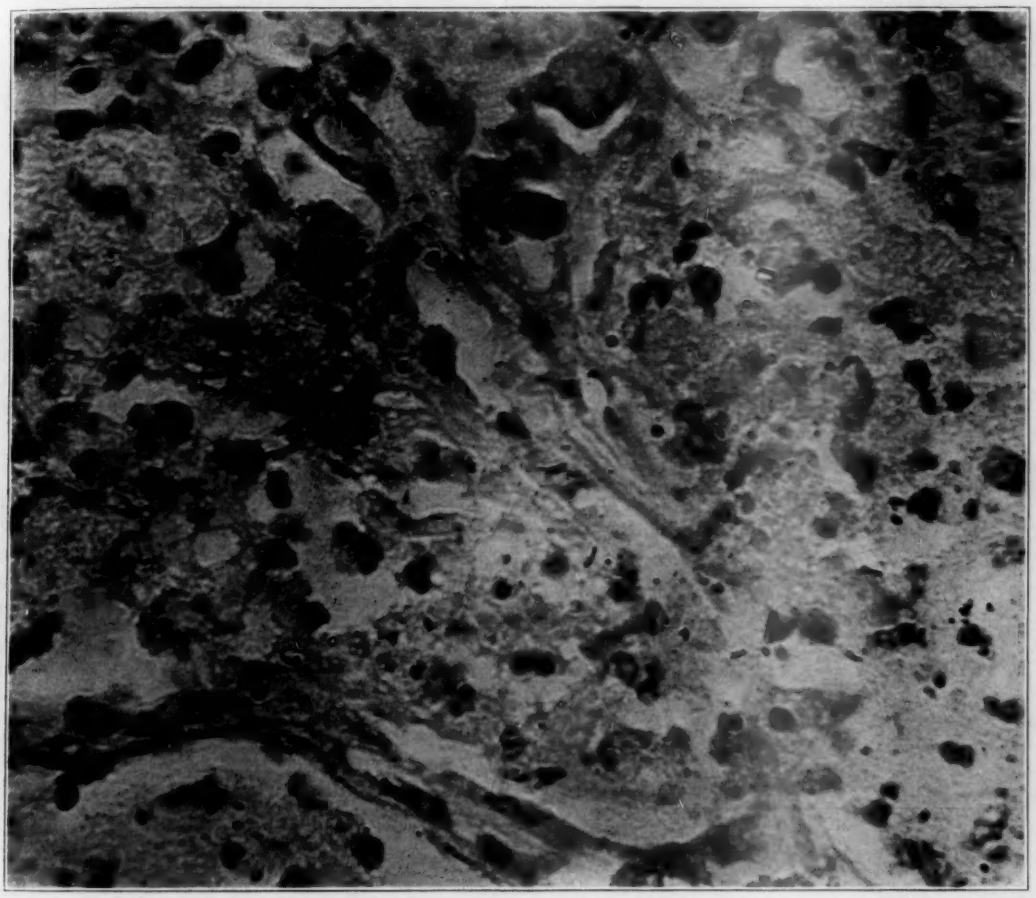

Fig. 3 (case 1).—Tuberculous pneumonia. Ziehl-Neelsen preparation showing an acid-fast organism.

devoid of a specific histology may caseate,[29] and, on the other, a number of important workers express their firm belief in the resolution of the characteristic gelatinous pneumonia.[30] As a matter of fact, Beitzke definitely stated that this form of infiltration can resolve completely.[15]

29. Orth, quoted by Fraenkel (footnote 18*b*, p. 693).
30. Müller, F., quoted by Duken (footnote 8*a*).

The tubercle itself—that paragon of tuberculous specificity—may undergo complete resolution. This rather astonishing fact has been repeatedly demonstrated in experiments on animals. Soper [31] injected a virulent strain of bovine tubercle bacilli, by way of the mesenteric vein, into rabbits previously infected with the H 37 strain (T. humanus), and obtained a miliary tuberculosis of the liver. Four of these animals were allowed to live fifty days and longer; the remainder had been killed at earlier intervals to observe the progress of the lesions.

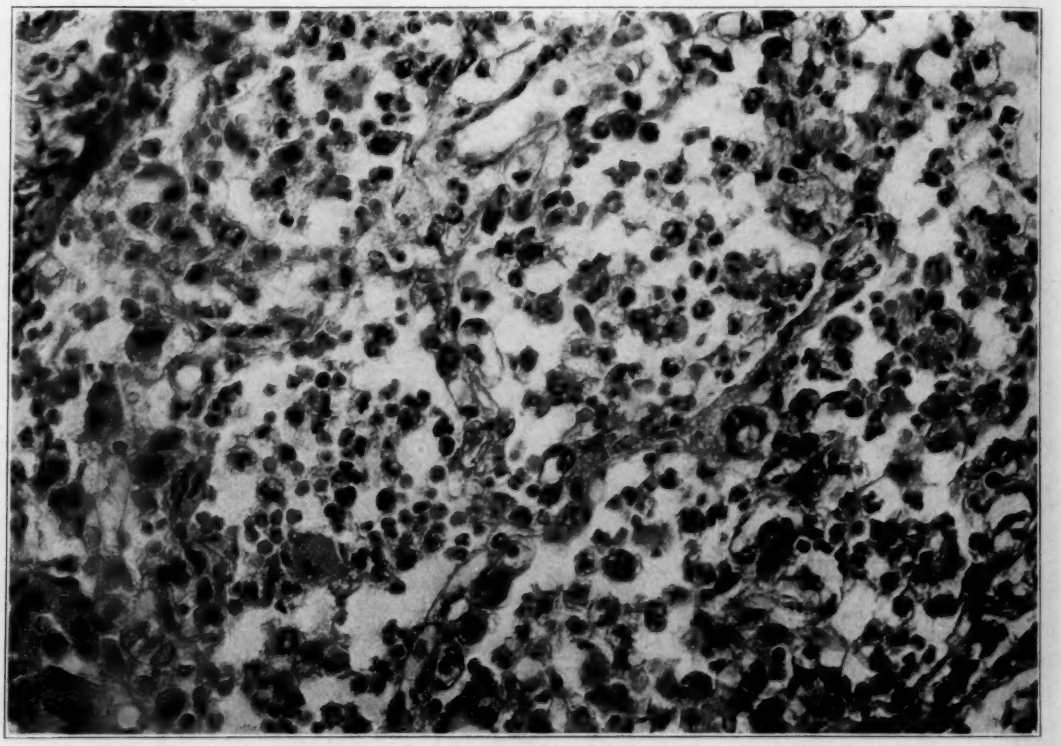

Fig. 4 (case 2).—Tuberculous pneumonia; reduced from a magnification of × 450.

Histologic examination of the fifty day group showed that the tubercles had almost entirely disappeared from the liver, although the livers of previously noninfected animals that had been inoculated in a like manner contained at that time many tubercles. Apparently the absorption of a pathologic tissue, which is accepted as classically characteristic of tuberculosis, had been complete, for Soper found no scarring or cirrhosis. There is here indubitable evidence of perfect resolution in allergic animals after reinfection with virulent bacilli.

31. Soper, W. B.: Am. Rev. Tuberc. **1**:385, 1917

Baldwin and Gardner [32] secured the same results in the lung by forcing guinea-pigs to inhale the R 1 strain of tubercle bacilli, a human strain which is known to produce a nonprogressive tuberculosis in these animals. A quotation from their publication will show how complete the resolution can be:

A primary generation of tubercles appears beneath the pleura. These progress to caseation, which is usually complete in the third or fourth week. The process of resorption which requires a variable length of time, from three months to over

Fig. 5 (case 2).—Tuberculous pneumonia; reduced from a magnification of × 125.

a year, is accomplished by the organization of the granulation tissue about the periphery of the tubercle, the gradual removal of the caseous matter, and the final absorption of the whole focus. Distorted alveoli are pulled in from the periphery and finally there remains a cluster of alveoli with thickened walls. Due to readjustment of the alveoli about the site of the former lesion the air spaces in the involved area again become normal in size and shape and all trace of the specific lesion is lost. In addition there is the nonspecific reaction of peripheral lymphoid hyperplasia which persists indefinitely and which is of great importance, as it may be the only trace of previous infection.

32. Baldwin, E. R., and Gardner, L. U.: Am. Rev. Tuberc. **5**:429, 1921.

The tracheobronchial lymph nodes become involved with proliferative tubercle within three weeks after infection. These lesions progress to caseation and then undergo fibrosis, in which condition they may persist for a long time and then be absorbed as in the lungs. The only trace of such a lesion is perhaps a moderate distortion of structure, the compression and obliteration of some sinuses and dilatation of others. The lymphocytes of the pulp are frequently replaced by reticuloendothelial cells. The progress of resorption is irregular; it may be complete within eighteen months or it may persist longer.

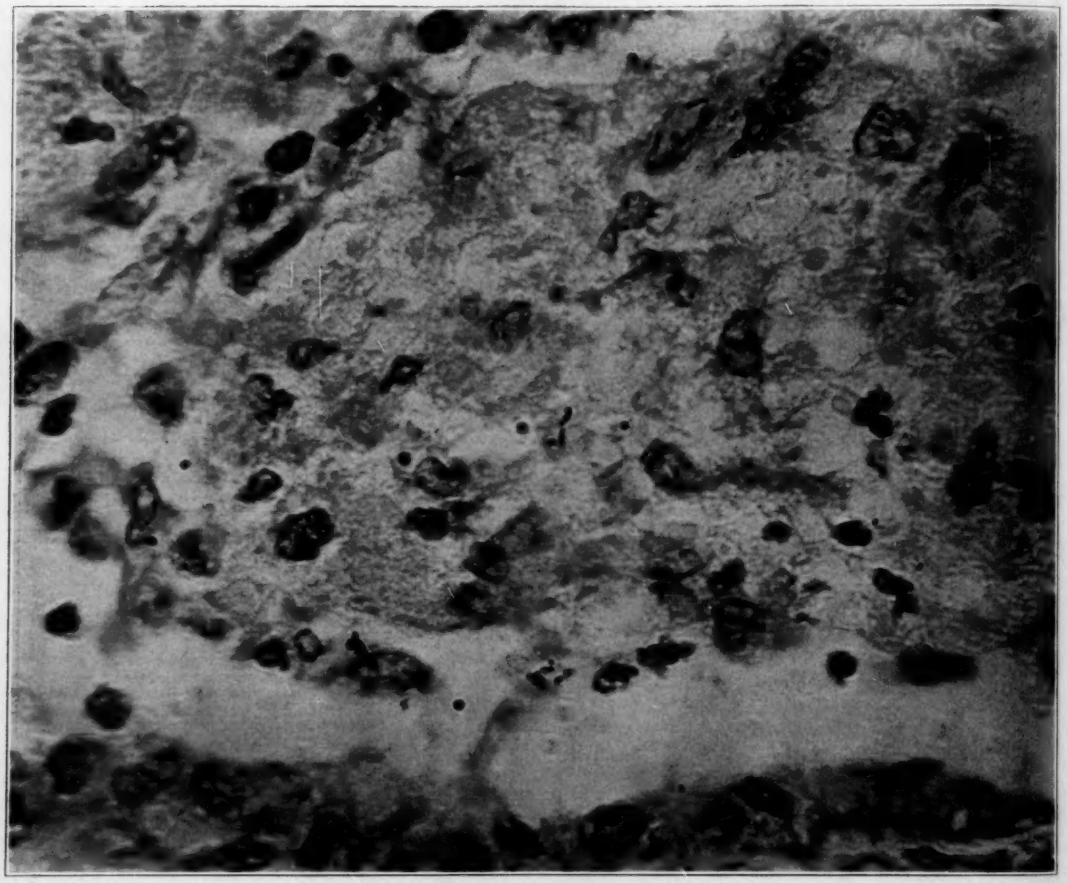

Fig. 6 (case 2).—Tuberculous pneumonia; Ziehl-Neelsen preparation, showing an acid-fast organism.

In animals reinfected with the same strain an abortive type of allergic reaction developed which also retrogressed, leaving almost no trace of its former presence.

In 1922, Gardner [33] repeated this study. He infected guinea-pigs by inhalation of the R 1 strain, and killed the animals at intervals of

33. Gardner, L. U.: Am. Rev. Tuberc. **6**:163, 1922.

from three weeks to seven months after having proved by means of the tuberculin test that they were infected. Here again, he showed that

> . . . the R 1 strain of tubercle bacillus is capable of producing lesions which progress to caseation, and that this caseation, together with the accompanying proliferation of fixed tissue cells, is then absorbed. The healing process is one of resolution, of which no trace remains at the site of the former lesion.

Rich [34] has published similar observations. He said:

> The tubercle may resolve and be completely absorbed, leaving no trace. This can occur only before connective tissue appears, but that it can and does occur is unquestionable. We have frequently observed this remarkable phenomenon. . . . This resolution is apparently neither preceded by, nor accompanied by necrosis.

Hence the pathologist will hesitate to lay down any dicta of prognosis on the basis of histologic criteria alone. He will not deny the possibility of a complete resorption of tuberculous exudates. Pathology will not be able to offer any more aid until the subject of this discussion is clearly defined and the inconsistency attendant on the present confusion of terms and meanings ceases. I do not think that terms with a pathologic connotation are at the present stage of the discussion feasible. If one examines these exudates—a purely clinical entity, as shown—from the clinician's standpoint, one finds but one factor that is common to all descriptions: the complete or almost complete resolution of a rather dense and homogeneous roentgenographic shadow in the lungs of persons suffering from pulmonary tuberculosis. All the other differentiating features which had been originally suggested have in the course of the decennium given way. In another contribution the attempt will be made to demonstrate on the basis of clinical studies that these resolving shadows in no way differ from the classic lesions of pulmonary tuberculosis except in their course. I wish to emphasize this point because it is of the utmost importance in evaluating the morphologic reports that have been published. Too often the fact that the resolution of the shadow is the essence of the subject has been ignored, and consequently most of the reports cannot be regarded as bearing directly on the discussion. Such a requirement can be satisfied only by a biopsy and a subsequent observation of the patient until complete resolution has set in. Most of the autopsy reports are really descriptions of residual stages from which one can reconstruct the original picture only by inference and probably with a high degree of error. The examination of a partially resolved exudate permits the rejoinder that the resolvable portion was the "nonspecific perifocal inflammation," whereas the nucleus, being "specific tuberculous" tissue, would not have resolved. Many of the published autopsies lack impor-

34. Rich, A. R., and McCordock, H. A.: Bull. Johns Hopkins Hosp. **44**:273, 1929.

tant data; even Rubinstein's [35] case, which fulfils the chief requirement ideally, is robbed of a coercive authority by the absence of a tuberculin test on the patient and a stain for tubercle bacilli on the excised tissue. Several of the reports give only vague descriptions of the gross appearance of the tissue; the frequent lack of a microscopic report is particularly distressing. In others the description is couched in general terms, often diagnostic and not descriptive, so that no critical review is possible. In my opinion Langer's [36] case, in which a reappearance of the shadow was involuntarily produced by the injection of tuberculin, is more valuable evidence of the specificity of the lesion than any of the published autopsies. The phenomenon that Langer observed and which has not infrequently been seen by those who have used the subcutaneous tuberculin test is a focal reaction; I cannot conceive of anything in the lung but specific tuberculous tissue giving this reaction. The cavitation described by Gerstenberger and Burhans [7] is also evidence in favor of the view that these exudates are specifically tuberculous. Indeed, these writers expressed just this opinion in 1927: "Those, however, that proceeded to the stage of cavity formation in the light of the present knowledge surely must for the time being be considered tuberculous."

With these limitations in mind, I shall discuss the published reports of autopsies on cases of "epituberculosis," i. e., resolving exudates. Only two—Rubinstein's case and that of Grävinghoff [37]—satisfy completely the clinical requirements of resolution of an extensive homogeneous infiltration associated with a manifest pulmonary tuberculosis. Rubinstein's [35] case is unique, since a biopsy of the infiltrated lung was made at the height of the patient's illness. The child recovered; the physical signs and the shadow in the roentgenogram disappeared. The clinical history and physical findings are quite characteristic of the resolving exudates. The roentgenogram is typical. It is unfortunate that Rubinstein at no place mentioned the results of a tuberculin test. Despite this serious defect, I cannot share the skepticism of Pagel and Henke.[38] Their suggestion that Rubinstein's case was a chronic pneumonia is improbable. A lobar infiltration of the density shown in the published roentgenograms, lasting considerably over one year, strictly delimited by the outlines of the right middle lobe, is distinctly a rarity in children, except as a result of tuberculosis. Chronic nontuberculous pulmonary disease is of an entirely different character and usually the result of diffuse bronchopneumonic lesions. The histologic report and the photomicrographs substantiate the diagnosis of tuberculosis. Giant cells which

35. Rubinstein, H.: Beitr. z. Klin. d. Tuberk. **70**:773, 1928.
36. Langer, H.: Ztschr. f. Kinderh. **34**:142, 1923.
37. Grävinghoff: Monatschr. f. Kinderh. **21**:447, 1921.
38. Pagel and Henke (footnote 23, p. 246).

are of the typical Langhans type, "exudate" cells, lymphocytes, fibroblasts and areas of caseation are certainly classic concomitants of tuberculous inflammation. It is unfortunate that Rubinstein did not carry out an acid-fast stain, a procedure that would have made his conclusions inescapable. In the absence of this absolute proof, one can only regard it in the highest degree probable that this was a true case of tuberculous pneumonia which went on to complete resolution.

In Grävinghoff's case one is not dealing with the resolving exudate itself but with its residuum. Over a year had elapsed since the infiltration had completely disappeared. The affected lobe was found in a state of "hepatization." Microscopic examination revealed only "an irregular and slight increase of connective tissue in the septums of the lobuli and alveoli." These observations probably describe the residual stage of many fugitive exudates. Grävinghoff's description is strikingly similar to the observations of Baldwin and Gardner [32] on guinea-pigs infected intratracheally with the R 1 human strain of tubercle bacilli.

In all other published cases there were merely large homogeneous infiltrations which remained stationary for many months. Death was due either to an intercurrent infection or to miliary tuberculosis. Since it is my opinion that the only true criterion of a resolving exudate, i. e., "epituberculosis," is its actual disappearance, these cases can claim no more than a resemblance to the usual course of such infiltrations. However, I believe that it is possible to demonstrate that the anatomic description of these lesions has revealed nothing new to the pathologist acquainted with and attentive to the vagaries of tuberculous inflammation.

Leitmann's [39] case was that of a child who had died of miliary tuberculosis after having had a homogeneous infiltration in the position of the right upper lobe for seven months. At autopsy this lobe was found to be firm; on cross-section the tissue was composed largely of connective tissue bands. There were several areas of caseous degeneration and a large cavity. Microscopic examination showed, in addition to many miliary tubercles, a considerable increase in connective tissue. The alveoli were in part atelectatic and in part "in a state of advanced desquamation."

Sonnenfeld's [40] case showed a chronic conglomerate tuberculosis. Some of the foci were partly caseated, others partly fibrosed, areas of bronchopneumonia. Between these foci were areas of pneumonia characterized by collections of lymphocytes and "exudate cells" in the state of fatty degeneration. The alveolar walls were fibrosed and edematous.

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39. Leitmann, J. S.: Beitr. z. Klin. d. Tuberk. **69**:606, 1928.
40. Sonnenfeld, T.: Beitr. z. Klin. d. Tuberk. **69**:209, 1928.

Eliasberg and Neuland [5] published the report of the first autopsy in a case of "epituberculosis." It is astonishing that the only information that their original article gives is that "there were no tuberculous changes in the lungs. The infiltration of the right upper lobe did not show the picture of gelatinous infiltration." In the "Handbuch der speziellen pathologischen Anatomie" Pagel and Henke [23] published a photomicrograph from this case. Their description spoke of "Tuberkelaehnliches Gebilde mit Riesenzellen (vom Typus Langhans)" (tubercle-like structures with giant cells of the Langhans type). If this photograph is carefully observed, one sees not only such cells but also the "exudate" cells so often found in tuberculous pneumonia. Hence, although it is quite true that this histologic evidence does not prove the tuberculous etiology, it puts the burden of the proof on those who deny such a diagnosis. It is probable that this case represents a true tuberculous pneumonia. Perhaps the case of Zadek [41] was a still earlier example, but unfortunately the only report that I could obtain is diagnostic in import rather than descriptive. Zadek said that at autopsy he found "a specific exudation of lymphocytes into the alveoli which was caused by the tubercle bacillus." The cases of Rubinstein, Sonnenfeld and Leitmann are probably developments, partly in the direction of necrosis, partly in the direction of repair and fibrosis. The final stage of a successful resolution is seen in the case of Grävinghoff.

Epstein's [42] case is manifestly one of primary infection in the left upper lobe with contiguous tubercles and collapse of the small amount of intermediate tissue. The picture of the gross specimen leaves no doubt but that this lesion is sufficient to explain the shadow in the roentgenogram. The morphology at death gives no guarantee that this intermediate tissue was not affected during the early stage of the process.

Engel [43] published three autopsies of "epituberculosis." Case 5 (Willie M.), as Engel himself stated, may have been a chronic non-tuberculous pulmonary disease. However, the child was only 18 months old, the tuberculin test was positive, and the roentgenogram shown is not characteristic of this disease. The author's report of the autopsy is meager, and there is no microscopic report; it is therefore impossible to judge the character of the "older and newer pneumonic processes" that Engel found.

Case 6 (Heinrich) is clinically not inconsistent with the diagnosis of a resolving exudate. The postmortem report was: "The right lung is firmly adherent, dense; on cross-section, it is a reddish gray and considerably indurated. Macroscopically it is free from tubercles." It is

41. Zadek, quoted by Klemperer, F.: Med. Klin. **23**:1957, 1927.

42. Epstein, B.: Jahrb. f. Kinderh. **99**:59, 1922.

43. Engel, S.: Berl. klin. Wchnschr. **58**:877, 1921.

important to compare this last statement with Engel's conclusion: "From an anatomic standpoint the indurated pulmonary tissue was free from tuberculosis." We do not believe that the important conclusions that Engel drew from his cases can be accepted unless his gross observations are fortified by microscopic examination of the tissue.

The clinical history in case 4 (Hubert W.) is so meager that it is not possible to discuss the diagnosis. The translation of the autopsy report reads: "The tissue (of the left lower lobe) is firm and fleshy and contains large tubercles which reach the size of a pea. A cheesy process extends in a pyramidal fashion from the hilus into the parenchyma. The hilus contains a row of totally caseated nodes. The right lung is thickly beset with larger tubercles." There is no description of any microscopic examination. Yet Engel concluded that this pneumonia was not tuberculous. In his discussion he said: "The tuberculous disease is localized to the left side. A pneumonia develops here which is abnormally located . . . and which runs a chronic course. It is not tuberculous. In this chronically tuberculous tissue, tuberculous lesions then develop." The last sentence evidently contains a misprint. From the context, it is evident that Engel wished to say: "In this chronically *pneumonic* tissue tuberculous lesions then develop."

In 1931 Goldberg and Gasul [44] published the clinical history and the autopsy report of a child with a tuberculous infiltration of the right upper lobe. In the course of eight months the infiltrate retrogressed. Following a severe reaction to a tuberculin test, an extraordinary exacerbation of the patient's symptoms occurred and the roentgenogram showed an infiltration of the entire right side of the chest. This the authors regard as a repetition of Langer's [36] experience. Again a reabsorption occurred. However, as the reproductions of the roentgenograms show, even at the period of greatest regression of the lesions, there was still an extensive homogeneous shadow in the right side of the chest. The case came to autopsy, and caseous mediastinal adenitis as well as a caseous bronchopneumonia of the right upper lobe was found. The nodes had eroded the bronchial wall at one point; it is therefore probable, although the authors did not mention such a condition, that there was also a bronchiogenic tuberculosis. From my previous comment it will be clear that this report suffers from the defects of its European predecessors. The lesion, particularly in its second phase, did not resolve to a greater degree than is commonly found in pulmonary tuberculosis in children. As I have pointed out, a practically complete resolution is the only dependable and characteristic feature of "epituberculosis." The autopsy report described merely the final state of those lesions still present at the time of death; from such a morphologic

44. Goldberg, B., and Gasul, B. M.: Am. Rev. Tuberc. **24**:285, 1931.

description one can learn little concerning the development of these lesions and nothing at all about those which had already resolved. The latter, alone, may with moderate assurance be termed "epituberculous."

From this review of the literature one can see that there is little information concerning the exact histologic character of the resolving lesions in pulmonary tuberculosis of childhood. It is not improbable that a certain percentage of the cases are casual commonplace pneumonias; some are atelectases, but the greater number directly depend on the action of the tubercle bacillus. Because of the evidence presented, I do not think it necessary to postulate any different mechanism for the pathogenesis of these lesions or any other histologic structure than those which have hitherto been known. They are probably tuberculous pneumonias which have fortunately stopped short of caseation. Nevertheless, not to prejudice any further investigative work and to give expression to the existing uncertainty as to the incidence of the definitely nontuberculous lesions, I propose for the entire group the term resolving or fugitive exudates in pulmonary tuberculosis.

Some workers have regarded these lesions as specific reactions, not to the tubercle bacillus itself, but to its metabolic products to which the body has become sensitized. This is the content of the term allergic exudates, which Duken [8a] suggested. There is no doubt but that a hypersensitiveness of the pulmonary tissue is a necessary factor in the development of the fugitive exudates. The primary infection occurs in virgin soil; the tissue is not specifically sensitized to the tubercle bacillus and its chemical constituents. This is probably the reason for the minuteness of the lesion, the slight surrounding inflammation and the ultimate state of characteristic morphology. Never again can the body react to the tubercle bacillus in this fashion; every subsequent defense will be conducted with a striking increase in the auxiliary phenomena of peripheral vascular dilatation and extravasation of the cellular and amorphous material which constitutes an inflammatory exudate. The second characteristic of hypersensitive tissue is its tendency to undergo the type of necrosis known as caseation. These characteristics are practically never again absent from any subsequent tuberculous lesions,[45] the extent of their manifestation in each case being determined by the location of the lesion and the particular reac-

45. These statements are true only if the dosage of tubercle bacilli is within a certain range, which again is dependent on the virulence of the strain and degree of allergy of the person infected. Rich (footnote 34, p. 311) attempted to express these complex relations succinctly in the arithmetical expression of variation $L \propto \frac{V\ N\ A}{R}$, when L equals the size of the lesion, V the virulence of the organisms, A the allergy of the person infected, R his resistance and N the size of the infecting dose.

tive ability of the invaded tissue, in short, the degree of allergy. Hence allergy is probably an essential condition of a fugitive exudate. This conception was clearly appreciated by Gerstenberger and Burhans [7] in 1927. They also realized that this allergy was an immunologic state of the entire organism, and called attention to the parallelism with the various types of cutaneous reactions to tuberculin. Fernbach,[46] in 1928, described acute tuberculous adenitis which he regarded as an equivalent of the allergic reactions in the lung. It is, however, not correct to assume that the response of the allergic organism is something *qualitatively* different from that of the insensitive body. Rich [47] has shown by experiments on animals that it is possible to produce the exudate characteristic of an allergic state in the nonsensitive guinea-pig, if the dose chosen is large enough; vice versa, the exudate of sensitive animals may approach that of the insensitive if the dose is small enough.

He said:

> That, following infection, the body acquires an altered reactivity or "altered attitude" toward the bacillus is unquestioned; but this altered activity is essentially quantitative rather than qualitative. It is not an accurate generalization to say that the reaction to the first contact with the bacillus is always tubercle formation, and that exudative inflammation never occurs in the allergic animal. Either the normal or the allergic animal can respond to the tubercle bacillus with either tubercle formation or exudative inflammation.

Pagel [48] has expressed essentially the same opinion. The studies of early cellular reaction to tubercle bacilli by Long, Vorwald and Donaldson [49] show the same fundamental trends in both normal and sensitized animals. The reaction characteristic of allergy is therefore merely the *state of an accelerated reactivity which was primarily native to the invaded tissue.*

These features of allergic inflammation can be reproduced by the injection of the chemically pure bacterial constituents that have been prepared by Anderson, Seibert and their respective associates.[50] A collection of monocytes in the typical form of the tubercle, the Langhans giant cell and even the central caseation may be produced by the injection of the bacillary fatty acid and phosphatide; the inflammatory exudate and coagulation necrosis, by the tuberculoprotein of Long and Seibert. These substances—the lipoid, protein and carbohydrate fractions—are probably the active constituents of tuberculin. These are the

46. Fernbach, H.: Monatschr. f. Kinderh. **42**:170, 1929.

47. Rich and McCordock (footnote 34, p. 281).

48. Pagel, W., in Engel and Pirquet: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, vol. 1, p. 213.

49. Long, E. R.; Vorwald, A. J., and Donaldson, L.: Early Cellular Reaction to Tubercle Bacilli, Arch. Path. **12**:956 (Dec.) 1931.

50. Long, Esmond R.: Am. Rev. Tuberc. **22**:467, 1930.

"toxins" of the tubercle bacillus. It is a misconception of the activity of this organism to assume that it has any other noxious faculties aside from those contained in the products of its own disintegration. It has been demonstrated beyond any doubt *which the facts on hand at present justify* that the tubercle bacillus has no true exotoxins. Its toxic qualities, therefore, must be equivalent to the sum of the poisonous substances of its own body. One is therefore not justified in differentiating between the noxious effects of the living bacillary body and those of its diffused toxins. The only difference that probably obtains between the local and peripheral effect of a focus of tubercle bacilli is that of the concentration of substances injurious to living cells. It is reasonable to suppose that in the immediate neighborhood of the bacilli the noxious effect will be the greatest and that its action will decrease in direct proportion to the distance. This is, in fact, the mechanism suggested by Tendeloo for the development of "collateral inflammation."[51] By injecting a solution of formic acid into the lungs of guinea-pigs he produced a central necrosis and concentric rings of inflammation and so reproduced the picture of the central nucleus and perifocal, viz., collateral, inflammation found in many tuberculous lesions. That the distribution is not always so regular is due, as Pagel suggested, to movements of the lymph stream, mechanical expression and flow along the broad surfaces of serous or mucous cavities. The possibility that some of the fractions of the tubercle bacillus may diffuse more rapidly and completely than others must also be borne in mind, although at present there is some evidence that this can occur only to a slight degree.[50]

Much of the confusion attendant on discussions concerning the pathogenesis of tuberculosis could be avoided if every writer on the subject would define his understanding of the term specific tuberculous tissue. It is clear that one can give it an etiologic connotation and hence regard all tissue changes produced by the tubercle bacillus as specifically tuberculous, or one may restrict it to those changes which conform to certain pathologic structures, such as the tubercle and caseous pneumonia. My understanding of the term is so well expressed by Pagel[52] that I can do no better than quote his views:

> From the pathologist's standpoint we consider as belonging to the tuberculosis of the guinea-pig, all the anatomic changes which the action of the tubercle bacillus in the tissue necessarily produces. It is immaterial to what forms the spontaneous or induced disease gives rise; the demonstration of the presence of tubercle bacilli, by what means whatsoever, and the knowledge that they themselves or in association with other agencies have produced these changes, determines the tuberculous nature of the process.

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51. Pagel, W.: Die allgemeinen pathomorphologischen Grundlagen der Tuberkulose, Berlin, Julius Springer, 1927, p. 61.

52. Pagel, W.: Beitr. z. Klin. d. Tuberk. **61**:643, 1925.

Doubtless there are several histologic structures that are accepted as typical for the action of the tubercle bacillus. They are, however, not absolutely specific for the effects of this bacterium,[53] nor do they exhaust the manifestations of its activity. In fact, there is certainly no doubt but that a large percentage of the diseased tissue in a tuberculous lung does not show these "typical" histologic forms. Indeed, Pagel said: "We can say that in many organs of the guinea-pig, even more so than in those of the human being, tubercles are rarities." [54] In the liver of the guinea-pig, for instance, Pagel found only the histologically nonspecific fibrotic tissue of cirrhosis; yet in the section he was able to demonstrate tubercle bacilli. Tubercle and caseous pneumonia are neither the only forms of tuberculous tissue nor, speaking quantitatively, the predominant forms. They are merely the norms of the activity of the tubercle bacillus on living tissue; under certain ideal conditions—with which one is at present only superficially acquainted—these norms are realized; more often they are merely approached, and hence tuberculous tissue shades off through infinite gradations into pathologic forms that can be understood etiologically and pathogenetically only when observed in conjunction with the other manifestations of tuberculotoxic activity or when studied functionally by serial animal experiment. It is therefore not an accident that the rigorists who hold to a strict anatomic standard of specificity should be found among the pure pathologists, whereas the experimentalists who have observed the versatility of the tubercle bacillus and watched the course of the disease through all its ramifications should have broadened their definition. The clinician who watches the ebb and flow of the infection through years feels profoundly dissatisfied with an anatomic interpretation that does not aid him in understanding the evolution of the disease and does not give him an anatomic groundwork for prognosis.[55]

SUMMARY

The frequency and prognostic importance of the resolving lesions in pulmonary tuberculosis of childhood have aroused the interest of many workers. Questions bearing on their etiology, pathogenesis,

53. Lubarsch, O., in Aschoff, L.: Pathologische Anatomie, ed. 5, Jena, Gustav Fischer, 1921, vol. 1, p. 547.

54. Pagel (footnote 52, p. 646).

55. C. A. Stewart, in an article entitled "Pulmonary Diseases: 5,816 Cases in Children" (Am. J. Dis. Child. **43**:803 [April] 1932), expressed the opinion that "epituberculosis" is merely a resolving tuberculous lesion. I cannot concur in his belief that this type of lesion is restricted to the stage of the primary infection. His article brings several references to resolving pulmonary lesions which are not mentioned in my publication, notably the article of T. C. Hempelmann, "The Prognosis of Pulmonary Tuberculosis in Infancy" (Am. Rev. Tuberc. **1**:99, 1917).

histologic characteristics and clinical diagnostic criteria are, however, still unsettled.

On the basis of a critical review of the literature and in the light of personal clinical and pathologic experience, the conclusion is reached that these lesions are of three types: (1) simple atelectases, (2) nontuberculous lobar or bronchopneumonias and (3) retrogressive tuberculous pneumonias. The exact relative incidence of the three lesions is not known, but it is probable that the retrogressive tuberculous pneumonias predominate. This is without doubt true for the lesions of long duration that lead to resolution. Since resolution is possible in almost every form of tuberculous inflammation, there is no reason for calling on any unusual mechanism to explain the retrogressive tuberculous exudates.

Clinically, the only reliable criterion for the diagnosis of the *retrogressive* type of tuberculous pneumonias is the course of the disease. This involves the ultimate complete or almost complete resolution of the process. The autopsies hitherto reported have dealt with the stage prior to possible resolution, or after resolution was complete, and therefore have contributed little to the solution of this problem. A decisive contribution would be made by repeated biopsy examinations, as in the case of Rubinstein.

In another contribution, clinical, roentgenologic and pathologic records will be presented which, it is believed, are in conformity with the ideas developed in this presentation.

Dr. Henry J. Gerstenberger, Director of Pediatrics of the Babies and Childrens Hospital, allowed me to use the material reported.

TETANY IN VERY YOUNG INFANTS

WITH SPECIAL REFERENCE TO ETIOLOGY

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NEW YORK

At present it is the almost universal belief that infantile tetany is a manifestation of rickets. Whereas in rickets the usual blood picture is that of a low inorganic phosphorus and normal calcium content, in tetany the reverse is true, the blood phosphorus being normal or increased and the blood calcium low.[1] The deficiency of the calcium ion has been proved to be the direct cause of the symptoms of tetany.[2] Huldschinsky[3] first showed, and others after him, that tetany was often a sequel of rickets inadequately treated. In a recent article Gerstenberger and his co-workers[4] demonstrated by means of roentgenologic studies and chemical analyses of the blood that interrupted or imperfect antirachitic treatment induced tetanic symptoms in the rachitic child. In their studies the presence of rickets was first proved by roentgenograms of the bones and by a low inorganic blood phosphorus. Insufficient ultraviolet therapy caused some healing of the rachitic bones, at which time the blood phosphorus rose, the blood calcium fell, and tetany ensued.

Experimentally, tetany has been induced in animals and in human beings by several procedures:[5] parathyroidectomy,[6] the administration

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From the Pediatric Service of Dr. Herman Schwarz, Beth Israel Hospital.

1. MacCallum, W. G., and Voegtlin: On the Relation of Tetany to the Parathyroid Glands and Calcium Metabolism, J. Exper. Med. **11**:18, 1919.

2. Howland, J., and Marriott, W. McK.: Observations on the Calcium Content of the Blood in Infantile Tetany, and upon the Effect of Treatment by Calcium, Quart. J. Med. **11**:289, 1918.

3. Huldschinsky, K.: Die Beeinflussung der Tetane durch Ultravioletlicht, Ztschr. f. Kinderh. **26**:207, 1920.

4. Gerstenberger, H. J.; Hartman, J. I.; Russell, G. R., and Wilder, T. S.: Etiology of Infantile Spasmophilia, J. A. M. A. **94**:523 (Feb. 22) 1930.

5. MacCallum, W. G.: On the Pathogenesis of Tetany, Medicine **3**:137, 1924.

6. Paton, D. N.; Findlay, L., and Watson, A.: The Parathyroids—Tetania Parathyreopriva, Quart. J. Exper. Physiol. **10**:243, 1916. MacCallum and Voegtlin (footnote 1). Howland and Marriott (footnote 2). Huldeschinsky (footnote 3). Gerstenberger, Hartman, Russell and Wilder (footnote 4). MacCallum (footnote 5).

of phosphates,[7] hyperventilation[8] and the induction of a state of alkalosis,[9] but the sole experimental tetany comparable with and similar to infantile tetany has been reproduced only after first rendering the animal rachitic. It is striking and significant that all those who were successful in superimposing tetany on rickets chose as their rachitic diet one with a high calcium-phosphorus ratio. This type of rachitic diet results in a form of rickets characterized by a low blood phosphorus and virtually normal blood calcium. Cavins[10] was able to effect tetany in rachitic rats by the simple process of fasting—a curative measure. Shohl and his co-workers[11] were able to produce tetany in rachitic rats by adding phosphate to the rachitic diet, and at the same time to produce signs of healing in the rickets. More recently, Hess and his co-workers[12] were successful in regularly inducing tetany in rats made rachitic with a diet having a calcium-phosphorus ratio of 4:1. To evolve tetany from rickets required from one to four days after the animal's diet had been changed to normal, which changed the abnormally high calcium-phosphorus ratio to normal, with subsequent healing of the rickets. It must be emphasized that in order to evolve tetany from rickets successfully, the dietary or therapeutic change must be abrupt and must bring about some healing of the rickets. In all these cases, as the phosphorus of the blood rose to a high or normal level, the blood calcium fell within the limits of tetany.

Clinical studies have thus shown the same sequence of events as those in experimental tetany of the infantile type. The chief difference is that, whereas the animal has been made rachitic by a specific diet, the child has not; that the tetany superimposed on the rachitic animal

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7. Binger, C.: Toxicity of Phosphates in Relation to Blood Calcium and Tetany, J. Pharmacol. & Exper. Therap. **10**:105, 1917. Salvesen, H. A.; Hastings, A. B., and McIntosh, J. F.: Blood Changes and Clinical Symptoms Following Oral Administration of Phosphates, J. Biol. Chem. **60**:311, 1924.

8. Grant, S. B., and Goldman, A.: Clinical Tetany by Forced Respiration, Am. J. Physiol. **52**:209, 1920.

9. Greenwald, I.: Alkalosis, Sodium Poisoning and Tetany, J. Biol. Chem. **59**:1, 1924. McCann, W. S.: A Study of the Carbon Dioxide Combining Power of the Blood Plasma in Experimental Tetany, J. Biol. Chem. **35**:553, 1918.

10. Cavins, A. W.: The Effect of Fasting (and Refeeding) on the Calcium and Inorganic Phosphorus in the Blood Serum of Normal and Rachitic Rats, J. Biol. Chem. **59**:237, 1924.

11. Karelitz, S., and Shohl, A. T.: Rickets in Rats: II. The Effect of Phosphate Added to the Diet of Rachitic Rats, J. Biol. Chem. **73**:665, 1927. Shohl, A. T., and Bennett, H. B.: Rickets in Rats: III. The Metabolism of Calcium and Phosphorus of Rats on Restricted Food Intake, ibid. **74**:247, 1927. Shohl, A. T., and Bing, F.: Rickets in Rats: VIII. Rickets in Tetany; Neuromuscular Response of Rats to Galvanic Stimuli, Am. J. Physiol. **86**:628, 1928.

12. Hess, A. F.; Weinstock, M.; Benjamin, H., and Gross, J.: The Induction of Tetany by Means of a Normal Diet, J. Biol. Chem. **90**:737, 1931.

has been effected by abrupt dietary changes or incomplete antirachitic treatment, while only the latter factor has been noted as effecting tetany in the rachitic child. Hamilton and his co-workers [13] have demonstrated that when rickets is being cured by any method, whether by abrupt changes in the diet of rachitic animals or by antirachitic measures of any kind, the rachitic blood serum at any given time can hold only a definite, lowered concentration of calcium and phosphorus. This lowered solubility product of calcium and phosphorus is fixed and probably maximal for a given rachitic serum.[14] Sudden changes from a rachitic to a normal diet or antirachitic treatment abruptly discontinued can initially produce a rise in blood phosphorus only at the expense of a fall in blood calcium. The rise and fall of blood phosphorus and calcium have the relationship of a logarithmic curve.[13] If the dietary changes and other measures curative in rickets are gradually instituted, time is allowed for the saturation properties of the serum (for calcium and phosphorus) to be increased. Then the blood can retain the added phosphorus without excessive sacrifice of the calcium. Proper antirachitic therapy restores to the blood its capacity to hold a high solubility product of calcium and phosphorus.

There seems little doubt, then, from laboratory and clinical evidence that infantile tetany may be and often is a sequel of imperfect healing of rickets. This is in accord with the well known fact that rickets is at its height in the winter and tetany in the late winter or spring, when rickets is being alleviated spontaneously but interruptedly by sunlight.[15] But is this the only mechanism of producing infantile tetany? In certain cases of tetany in very young infants the evidence is at variance with much that has just been described. Three examples of tetany which seem to have a different pathogenesis are here reported in detail with roentgenologic and chemical studies of the blood.

REPORT OF CASES

CASE 1.—*History.*—M. A., a boy, 2 months old, was admitted to the hospital on Nov. 19, 1930, and discharged on December 11. The chief complaint was convulsions of nine days' duration. The patient was one of twins; there were no other children in the family. Both parents were free from disease, but the mother had had three miscarriages.

13. Hamilton, B.; Kajdi, L., and Meeker, D.: The Effect of Phosphates Administered, Antirachitic Treatment and Spontaneous Healing on the Calcium in the Serum of Rachitic Rabbits, J. Biol. Chem. **88**:331, 1930.

14. Holt, L. E.; LaMer, W. K., and Chown, H. B.: Studies in Calcification: The Solubility Product of Secondary and Tertiary Products Under Various Conditions, J. Biol. Chem. **64**:509, 1925.

15. Hess, A. F., and Lundagen, M. A.: A Seasonal Tide of Blood Phosphates in Infants, J. A. M. A. **76**:2210 (Dec. 30) 1922.

16. Reference deleted by author.

The child was born normally at full term. The birth weight was 4 pounds and 10 ounces (2,050 Gm.). He had been artificially fed from birth. The last formula was milk, 20 ounces (591.4 cc.); water, 10 ounces (295.7 cc.), and dextrimaltose no. 2, 3 tablespoonfuls. He had received orange juice, but no cod liver oil or viosterol. Ten days before admission he had three series of convulsions, each of

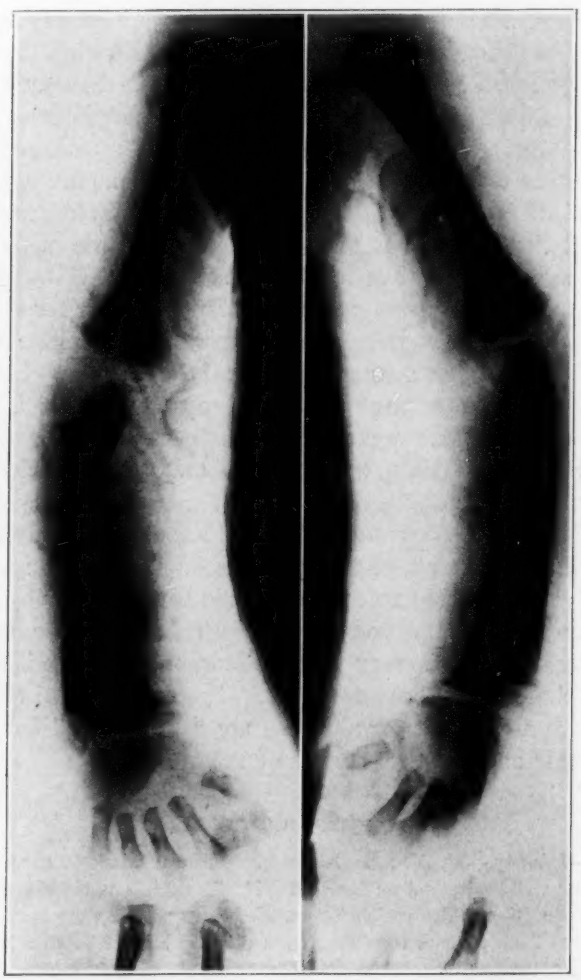

Fig. 1 (case 1).—Roentgenograms taken on Nov. 20, 1930, the day after the patient's admission to the hospital, showing slight cupping and flaring of the epiphyseal end of the ulna, characteristic of early rickets as determined roentgenologically.

one-half hour's duration. The next day the convulsions recurred. With simple sedative treatment, he was free from convulsions for the next five days; then they again recurred. Another day free from convulsions followed, but the day before admission they were frequent and violent, taking place within an interval of only

a few minutes. There was no fever or infection. The child had been eating well, and had had no gastro-intestinal disturbance until two days before admission, when he vomited a few times.

Examination.—Physical examination showed a small, immature, pale infant in carpopedal spasm, interrupted by frequent marked tonic and clonic convulsions. The anterior fontanel was normal, the posterior one closed. There was no craniotabes or beading of the ribs. The eyes, ears, nose and throat were normal. The lungs and heart were normal. The liver was barely palpable. No other viscera or masses were palpable. Neurologic examination showed markedly positive Chvostek and Trousseau signs. The reflexes were hyperactive. The temperature was 99 F., and the weight was 7 pounds and 8 ounces (3,400 Gm.).

The diagnosis of infantile tetany was made.

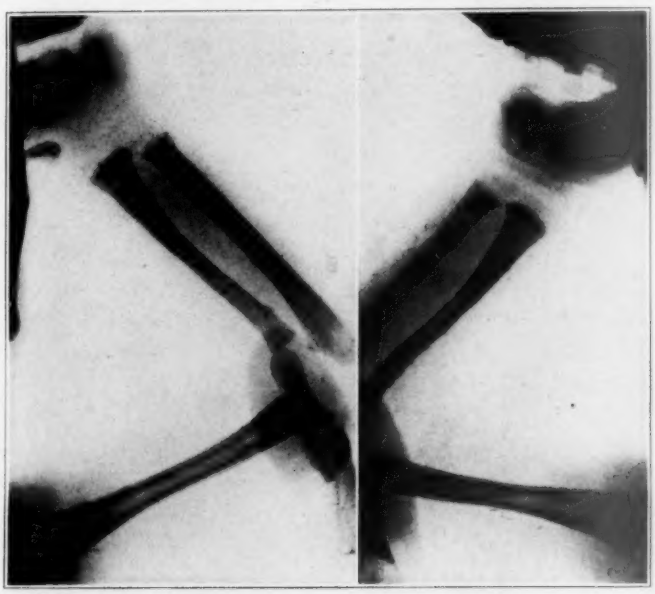

Fig. 2 (case 1).—Roentgenograms taken on Dec. 10, 1930, the day before discharge from the hospital, showing increased calcification of the epiphyses indicative of the healing of the patient's rickets; cupping is still present.

The results of chemical analyses of the blood were:

Date	Blood Calcium, Mg.	Blood Phosphorus, Mg.	Product
11/20	Specimen inadequate		
11/22	6.8	7.2	49.0
12/ 2	9.6	3.7	32.8

Treatment.—The treatment consisted of 20 drops of viosterol and 30 grains (1.95 Gm.) of calcium lactate daily. The convulsions continued for two or three days, and then rather suddenly ceased.

Ronetgenograms demonstrated that the epiphyseal end of the ulna showed slight cupping and flaring. The juxta-epiphyseal line was not frayed, was sharply defined

and regular. There was a moderate degree of bone atrophy and a general decrease in ossification as shown by the delayed appearance of carpal centers and the irregular formation of epiphyses of the knee joints. The bones also showed further evidence of malacia in the slight degree of bowing and lamellation of the cortex. There was evidence of mild rickets.

CASE 2.—*History.*—L. M., a boy, 2 months old, admitted to the hospital on Nov. 19, 1930, and discharged on December 11. The history of this baby was exactly the same as that of his homologous twin, except that his weight at birth

Fig. 3 (case 2).—Roentgenograms taken on Nov. 20, 1930, showing slight cupping and flaring of the epiphyseal end of the ulna similar to that of case 1.

was a little less, 4 pounds and 6½ ounces (1,990 Gm.). The feeding history was the same as the brother's. The onset of the convulsions, their recurrence, the periods free from convulsions and the later frequent violent convulsions were simultaneous in both children. These twins on investigation were found to be one ovum twins, and their anthropometric measurements taken at a later date were virtually the same.

In the hospital, the coincidence of the convulsions in the twins was a most remarkable sight. When one had a convulsion, a convulsion in the other was certain to follow. Slamming of the door of their room or any other sharp stimulus sent both twins simultaneously into an eclamptic state. It was as if both children

were joined to one high explosive fuse. The convulsions stopped as well as started together. The second twin was given exactly the same treatment. It was difficult to say which one was cured first.

The roentgen reports of the bones were the same as those of his twin brother's.

The diagnosis of infantile tetany was made.

The results of chemical analyses of the blood were:

Date	Blood Calcium, Mg.	Blood Phosphorus, Mg.	Product
11/20	7	Quantity not sufficient	
12/ 2	10	3.7	37

The follow-up study of these children revealed no signs of rickets one and two months later. They had received viosterol since discharge from the hospital.

Fig. 4 (case 2).—Roentgenograms taken on Dec. 10, 1930; the increased calcification of the epiphyses shows the healing of recent rickets.

CASE 3.—*History.*—J. C., a boy, 7 weeks old, was admitted to the hospital on Jan. 30, 1931, and discharged on February 28. The chief complaint was convulsions for two days.

The patient was the first child of his parents, both of whom were healthy. He was born prematurely but normally, weighing 4 pounds and 15 ounces (2,250 Gm.) at birth. The baby never took the breast, and was fed irregularly mixtures of milk, water and sugar. There had been no previous infection.

Two weeks before examination cough and fever developed, which the family physician diagnosed as grip. In three or four days, the child was apparently well, but still had a nasal discharge. The day before admission he began to have generalized convulsions, to the number of eight or nine before admission. There was no vomiting or diarrhea. No viosterol or any other antirachitic therapy had ever been given.

Examination.—Physical examination showed a small, immature, pale infant, having generalized convulsions. He was not cyanotic or drowsy. Craniotabes was present to a 1 plus degree, as well as slight beading of the ribs. The fontanels, ears, nose and throat were normal. The heart and lungs were normal. The abdominal examination gave negative results, except for a palpable liver. The Chvostek and Trousseau signs were positive. The temperature was 99.6 F. The urine showed a very faint trace of albumin, and secondary anemia was present, with a hemoglobin content of 53 per cent.

The diagnosis of infantile tetany was made.

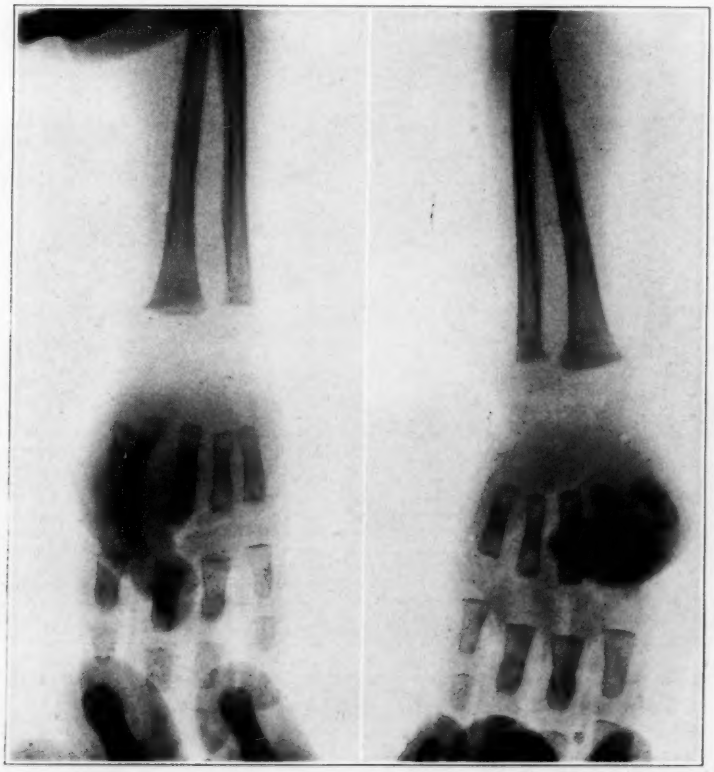

Fig. 5 (case 3).—Roentgenograms taken on Feb. 4, 1931, five days after admission to the hospital. There are no roentgenologic signs of rickets. The bones show a moderate degree of osteoporosis.

Chemical analyses of the blood gave the following results:

Date	Blood Calcium, Mg.	Blood Phosphorus, Mg.	Product
1/31	6.8	6.2	42.0
2/ 4	7.4	6.6	48.8
2/17	8.2	3.7	31.0

Treatment.—The treatment was calcium lactate, 30 grains (1.95 Gm.) daily, which was soon increased to 60 grains (3.9 Gm.) daily; the convulsions continued

but in a milder form. Viosterol, 20 drops daily, was administered throughout hospitalization, and calcium gluconate was later substituted for the lactate. On February 14, when the blood calcium was 8.2 mg., there were no convulsions, but latent tetany was present, as indicated by the positive Chvostek and electrical reactions. On February 16, all therapy was discontinued for experimental purposes, but the tetany proceeded uneventfully to a full cure with normal electrical reactions.

Roentgen examination showed no rachitic changes within the juxta-epiphyseal area of the bones of the forearms. There was atrophy of bone with lamellation of the cortex. The epiphyseal lines were sharply defined, with no cupping and no striation of the juxta-epiphyseal ends.

The diagnosis then made was atrophy of the bone with no evidences of rickets.

A follow-up study of this child revealed the development of mild rickets, as indicated by craniotabes, and a mild rachitic rosary, with flaring of the ribs.

COMMENT

Several features are common to these cases. The symptoms of tetany began at 7 weeks of age in infants predisposed to it by virtue of being twins or prematurely born. Physical examination showed early rickets in the premature child and no demonstrable rickets in the twins. All three showed osteoporosis, and on roentgen examination signs of rickets were present in the twins. The initial blood calcium was low and the blood phosphorus was high, the latter observation being not uncommon in tetany.[17] With the cessation of symptoms, the blood calcium rose and the phosphorus fell, again exemplifying the logarithmic relationship of their solubility product in blood serum. As a matter of fact, during the curing of the tetany, the blood phosphorus and the calcium-phosphorus solubility product fell to actually rachitic figures.[18] This was the converse of what occurred when tetany was superimposed on rickets. It almost seemed that from this type of tetany frank rickets could be produced, judging by chemical studies of the blood.[18] It must be borne in mind that not only was antirachitic therapy suddenly unloosed on these babies, but that calcium salts in fairly large doses were being administered, constituting a high calcium diet. Recall how the addition of phosphates had caused tetany in animals made rachitic by a high calcium diet.

Quite striking was the seasonal occurrence of the tetany. The twins were stricken in November (fall tetany) and the premature child in January. The cases in November were without clinical signs but showed roentgen evidence of rickets, while the case occurring in winter showed evidences of early, mild rickets; none had a suggestion of a

17. Marples, E., and Crump, E.: High Phosphorus Concentration in Infantile Tetany, Am. J. Dis. Child. **39**:533 (March) 1930.

18. Howland, J.: Etiology and Pathogenesis of Rickets, Medicine **2**:368, 1923. Howland, J., and Kramer, B.: Calcium and Phosphorus in the Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

healing process. Powers [19] in his case report of tetany in a very young infant stated that he found no clinical or roentgen evidence of rickets. That rickets can be proved at such a tender age was demonstrated from the same clinic by Dunham [20] in an even younger infant. The remarkable response of these patients to relatively small doses of viosterol (20 drops daily) is also presumptive evidence that this tetany is a manifestation of rickets.

It seems safe to assert that the common suprarachitic pathogenesis of tetany was not present in these cases. Some years ago Shipley, Park, McCollum and Simmonds [21] stated that rickets with tetany and rickets without tetany were two distinct forms of metabolic disturbance. These authors produced by different ratios of calcium and phosphorus two types of rickets, one with a low blood phosphorus and the other with a low blood calcium. The first kind of rickets was never, per se, concomitant with active tetany (though it might follow the healing stage); the low calcium type was sometimes associated with active tetany. Their report did not reveal the complete chemical figures or the level to which the calcium fell in the low calcium form of rickets. The present study, however, leads to a similar conclusion, that this form of tetany is a contemporaneous expression of primary rickets due to a low calcium diet, distinct from the rickets due to a low phosphorus diet from which tetany may eventuate only as a sequel. Certain very young infants are predisposed to this form of rickets with tetany, which may result from the sharp nutritive changes of extra-uterine life.

The patients studied had evidences of rickets. A type of rickets characterized by a high blood phosphorus and low blood calcium [22] has been known to develop in the rachitic premature child. This condition is accentuated if a poor state of nutrition supervenes, for Finkelstein,[23] Hess [24] and others have made the clinical observation and stressed the fact that the undernourished premature child is more prone to tetany than to mere rickets. This is not surprising when one recalls that the major portion of calcium is deposited in the fetus in the last three months of pregnancy.[25] This holds true for other minerals in addition

19. Powers, G. P.: Tetany as a Cause of Convulsions in Very Young Infants, J. A. M. A. **84**:907 (June 20) 1925.

20. Dunham, E. C.: Rickets in an Infant of Thirty-Four Days, Am. J. Dis. Child. **26**:155 (Aug.) 1923.

21. Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, N.: Is There More Than One Kind of Rickets? Am. J. Dis. Child. **23**:91 (Feb.) 1922.

22. Hess, A. F.: Rickets, Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929, p. 211.

23. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, Julius Springer, 1924, p. 526.

24. Hess (footnote 21, p. 367).

25. Hess (footnote 21, p. 145).

to calcium. Consequently, the premature child is born with a mineral deficiency which is shown by thinner, more rarefied bones on roentgen examination, as in my cases. Rosenstern [26] even demonstrated that almost all premature children have a hyperirritability of the nervous system to the galvanic current, indicating a latent tetany. It seems to us that the tetany of these children is a primary expression of rickets, and in no way related to any healing process. This may be a clinical facsimile of the low calcium form of rickets produced by Shipley, Park, McCollum and Simmonds.[21]

A human counterpart of this type of rickets has been doubted by some, but definite rickets of a mild nature with low blood calcium and tetany as a primary expression fits the description of low calcium rickets. It is well known that this type of rickets never shows marked roentgenologic evidence of being present, and is in that respect also different from the form of rickets due to a low phosphorus diet, which is the form that commonly develops in the infant. Because of the sparseness of roentgenologic evidence, the rickets peculiar to the premature child and also to atrophic children has sometimes been called passive rickets.[22]

The twins revealed evidence of rickets on roentgen examination. They also showed an osteoporosis with a low blood calcium and tetany. Twins, like premature children, are born with a marked calcium and mineral deficiency. Is this expressed in a low blood calcium which may lead to tetany? Experimentally, tetany has been produced in animals by means of a low calcium diet.[27] Histologic examination of the bones of these animals showed osteoporosis but no rickets. Osteomalacia and celiac disease are both characterized by calcium deficiency with rarefaction of the bones and a low blood calcium, which often leads to tetany.[28] Yet the signs of rickets are usually absent.[29] The clinical tetany that the premature child in this study presented conforms in some respects to this mode of causation. While the excellent response of the tetany to viosterol is suggestive of a rachitic basis, this is by no means conclusive evidence. On the other hand, osteoporosis possibly predisposes to rickets, and in atrophic children the presence of rickets may not be manifested clinically or roentgenologically. The osteoporosis is a substitute, so to speak, for rickets in some undernourished children.

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26. Rosenstern, J.: Zur Wirkung des Leberthrans auf Rachitis und Spasmophile Diathese, Berl. klin. Wchnschr. **47**:822, 1910.

27. Hess (footnote 21, p. 370).

28. Lehndorff, H., and Mautner, H.: Die Coeliakie, Ergebn. d. inn. Med. u. Kinderh. **31**:456, 1927. Parsons, L. G.: The Bone Changes Occurring in Renal and Coeliac Infantilism and Their Relationship to Rickets: III. Celiac Rickets, Arch. Dis. Child. **2**:198, 1927.

29. Hess (footnote 21, p. 362). Lehndorff (footnote 27, first reference).

Even osteomalacia may be a form of rickets at a different stage of life.[30] If this point of view is taken, the rickets is a primary form due to a low calcium diet and associated with tetany. The other concept, to regard the tetany of the premature child as the expression of a primary calcium deficiency with osteoporosis, possibly without the presence of rickets, cannot with certainty be dismissed. In any event, the mechanisms for the pathogenesis of infantile tetany are different from the usual concepts gleaned from recent pediatric literature on tetany evolving from a healing phase of rickets.

SUMMARY AND CONCLUSIONS

1. Tetany occurring in very young premature infants may be the primary expression of a low calcium form of rickets, and may not be suprarachitic, as in older infants.

2. Tetany in very young immature infants with no clinical or roentgen evidence of rickets but with evidences of osteoporosis may possibly be a nonrachitic form of tetany. A congenital deficiency in calcium may develop into the type of infantile tetany comparable to that resulting from osteomalacia and celiac disease.

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30. Hess (footnote 21, chap. 13).

Case Reports

THE ARTHUS PHENOMENON

A SEROLOGIC STUDY IN A SYPHILITIC CHILD WITH A FATAL REACTION TO TRANSFUSION

I. HARRISON TUMPEER, M.D.

With the Technical Assistance of

ELIZABETH J. COPE, S.B.

CHICAGO

In 1903, Arthus [1] observed a characteristic set of changes in rabbits given subcutaneous injections of horse serum at intervals of several days which has since been known as the Arthus phenomenon. The reactions become successively worse after the third inoculation. The local reaction varies from slight infiltration persisting two or three days to induration, edema and thickening lasting several weeks; after the seventh or eighth injection, the area becomes aseptically gangrenous and cicatrizes with difficulty. It is noteworthy that the injections are not made at the same site. It seems that the anaphylactic antibodies react with the specific antigen, which results in a toxic substance or substances, judging by the local effects in the tissue. Arthus demonstrated that these changes were not the result of pressure, because the same phenomenon was observed with the injection of 1 cc. of serum or less as long as the interval of several days was observed. On the other hand, the volume of the serum played no rôle, because 10, 20 or 40 cc. of the same serum had no effect when injected at frequent intervals. The reaction is specific for the antigen used.

It is natural to inquire whether such changes occur in man. It would seem that if experimental conditions were observed, such a phenomenon might be produced. As long ago as 1909, Lucas and Gay [2] called attention to similar effects in children inoculated at three week intervals with 1,500 units (5 cc.) of diphtheria antitoxin as a routine prophylactic measure in the Children's Hospital of Boston. They concluded that the reproduction of the Arthus lesions in children completed

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1. Arthus, M. M.: Compt. rend. Soc. de biol. **55**:817 (June) 1903.

2. Lucas, W. P., and Gay, F. P.: J. M. Research **20**:251 (April) 1909.

the analogy between serum sickness in man and serum anaphylaxis in animals. This observation remained unnoticed until recently, probably owing to the fact that the repeated administration of antitoxin was not a common practice. With the advent of the toxin-antitoxin era a new situation developed in which sensitization to horse serum was produced by three injections at weekly intervals of the minute quantities of horse serum present in the ordinary toxin-antitoxin mixtures used until recently. Undoubtedly subsequent reactions in the nature of the Arthus phenomenon occurred following additional use of horse serum for other reasons, but they were disregarded or not sufficiently appreciated until 1927. In that year Gatewood and Baldridge [3] described six cases of varying intensities of reaction, the severest of which, occurring in a nurse of 25, so closely parallels our case, occurring in a girl of 5, that the descriptions are interchangeable.

PURPOSE OF REPORT

Although a full clinical report of this case has been published elsewhere,[4] the bizarre serologic manifestations necessitate recording separately, because there is no previous similar study, owing to the rarity of the condition or the failure of its recognition, and because these serologic changes are too striking and significant to be concealed in a general report.

CLINICAL DATA

Briefly, the pertinent facts are as follows:

A girl of 5 years had received the usual three inoculations of horse serum toxin-antitoxin in the gluteal areas at weekly intervals in 1926.

On March 27, 1930, she received 1,000 units of diphtheria antitoxin in the left gluteal region because of contact with a brother with diphtheria. Within a few hours the injected area became red and swollen. The next day there were urticarial lesions locally, which became more scattered the second day, and at this time a sore throat and fever developed.

On March 30, 15,000 units of diphtheria antitoxin was injected into the right gluteal region because the throat culture contained diphtheria bacilli. It is significant to note that the local reaction from the preceding injection was still present.

Within three hours the last area became enormously swollen, and a purplish spot appeared in the center surrounded by similar satellite areas.

For the next five days the following changes occurred: The purpuric spots coalesced to cover the entire buttock. A spot appeared in the popliteal space, and the right knee became swollen and tender with limitation of motion. The right lower quadrant of the abdominal wall became mildly indurated, and the process

3. Gatewood, W. E., and Baldridge, C. W.: Tissue Hypersensitiveness Following the Administration of Toxin-Antitoxin: Phenomenon of Arthus, J. A. M. A. **88**:1068 (April 2) 1927.

4. Tumpeer, I. Harrison; Matheson, A., and Straus, D. C.: Arthus Phenomenon in a Syphilitic Child, J. A. M. A. **96**:1373 (April 25) 1931.

extended beyond the midline to the left side. The right labium shared in this change. On the fifth day, the entire area of the buttock was purple, and the abdominal wall was more swollen. The symptoms in the knee began to subside.

On the seventh day, the gluteal area became pink, as though the tissue were resuming vascularity.

On the eighth day, the region became black, and the eschar began to sink below the surface of the healthy tissue.

On the ninth day, bullae filled with a serous fluid formed around the periphery. From this time the gangrenous mass separated itself sharply from the healthy areas so that the mummified area was a distinct mass.

On the twelfth day, bulging had appeared so far in the right lower quadrant that an incision was made, yielding considerable thick yellow pus containing a gram-positive diplococcus. The slough finally exposed the muscles of the region, giving the appearance of an anatomic dissection. The fascia had disappeared in the slough. The gangrenous area was removed surgically, and the wound treated locally. By this time the skin and subcutaneous fascia of the thigh were so undermined that the lesion of the buttock communicated with a drainage opening in the popliteal space.

During all this time, the child's temperature ranged between 99.6 and 101 F. The respiratory rate ranged from 28 to 36, and the pulse rate, from 110 to 140. The urine was alkaline, with a trace of albumin, and contained many pus cells. The patient perspired profusely and was markedly pale. The blood culture was negative. On the fourteenth day, the red cells numbered 3,750,000; hemoglobin, 60 per cent, and white cells, 14,900, with polymorphonuclears 78 per cent, lymphocytes 19 per cent and monocytes 3 per cent. One week later the blood findings were the same, except that the white cells numbered 22,700, with polymorphonuclears 68 per cent, lymphocytes 24 per cent, monocytes 8 per cent and no eosinophils. There were no eosinophils in smears of the pus, although the fields were filled with polymorphonuclear leukocytes and bacteria. At this time it was found that the Wassermann reaction was 2 plus and the Kahn reaction 4 plus.

On account of the general weakness and anemia, on the twenty-sixth day the child was given a transfusion of 250 cc. of blood from a compatible donor, group I (Jansky), by the syringe method under local anesthesia into the right cephalic vein. Within an hour the child manifested shock, became cyanotic, vomited and became unconscious. She rallied following stimulants and removal to an oxygen tent, although her pulse rate ranged from 160 to 170. She spoke a few words, asked for dinner in a semidelirious state, drank a few ounces of water and died about three hours after the transfusion. The donor had been frequently used at the hospital, and it was reported that his blood had caused no reactions previously. He had never received foreign serum.

SEROLOGIC DATA

The following tables illustrate the procedures employed and the results obtained with the blood of the patient and of controls.

Controls.—The sister was especially pertinent as a control because she had had three weekly inoculations of horse serum toxin-antitoxin from the same batch and at the same time as the patient and a prophylactic inoculation of 1,000 units of diphtheria antitoxin at the same time and from the same lot as the patient; she likewise had a positive Kahn reaction despite the nonsyphilitic clinical appearance. She had not reacted to the 1,000 units of antitoxin with a local reaction and had

not received a fifth injection of horse serum, and her Wassermann reaction was negative, but her Kahn reaction was only slightly less positive than that of the serum of the patient. The brother was valuable as a control because he had also had toxin-antitoxin, although not at the same time or of the same lot. He had had a fourth injection of horse serum in the form of 15,000 units of diphtheria antitoxin at the same time that the patient received her fourth injection of 1,000 units. He manifested no reaction, while urticaria developed in the sister, as previously noted. The brother had an indeterminate Kahn and a negative Wassermann reaction. Further controls consisted of the donor's serum, a known syphilitic serum of the same blood grouping, type I Jansky, diphtheria antitoxin and saline solution.

TABLE 1.—*Results of Tests on the Blood of the Patient and That of the Subjects Used as Controls*

		Wassermann		Horse Serum Precipitins			
Serum	Kahn	Cholesterol	Lipoid	Kahn	Hektoen (Ring)	Blood Group Jansky	Schick
Patient	++++	++	—	++	1:32	1	—
1. 1926, horse serum toxin-antitoxin							
2. 1926, same 7 days later							
3. 1926, same 7 days later							
4. 1930, March 27, 1,000 units of diphtheria antitoxin							
5. 1930, March 30, 15,000 units of diphtheria antitoxin							
Sister	+++	—	—	..	—	..	..
1. 1926, horse serum toxin-antitoxin							
2. 1926, same 7 days later							
3. 1926, same 7 days later							
4. 1930, March 27, 1,000 units of diphtheria antitoxin							
Brother	+—	—	—	..	—	..	..
1. 1928, horse serum toxin-antitoxin							
2. 1928, same 7 days later							
3. 1928, same 7 days later							
4. 1930, March 27, 15,000 units of diphtheria antitoxin							
Positive syphilitic	++++	++++	++++	..	..	1	..
Donor	—	—	—	—	—	1	..

Syphilis.—The positive reactions for syphilis without clinical manifestations were explained by the fact that the father had brought the disease home during the preceding year, infecting the mother and children. The mother volunteered the significant comment that the patient was unusually attached to the father and constantly "hung on his neck." By the same laboratory technic, the serum of the donor was negative and the known syphilitic serum was strongly positive, or 4 plus, in both Kahn and Wassermann tests with two antigens.

Precipitins.—The positive reaction to the precipitin test with horse serum obtained with the patient's serum is interesting in the light of the observations of Cooke and Spain,[5] who found that precipitin bodies are absent in naturally sensitive human beings, are present in some artificially sensitized human beings and are always present in artificially sensitized animals. The negative findings in the

5. Cooke, R. A., and Spain, W. C.: J. Immunol. **17**:295 (Oct.) 1929.

almost identically treated brother and sister indicate that the patient alone had become artificially sensitized to horse serum. It is likewise to be noted that there were no precipitins to horse serum in the donor's serum.

Schick Test.—The negative reaction to the Schick test obtained with sheep serum toxin-antitoxin demonstrates the absence of a cutaneous reaction to sheep serum and indicates, incidentally, that the patient's serum contained more than $\frac{1}{30}$ unit of antitoxin per cubic centimeter.[6] The latter is easily explained by the antitoxin administered, leaving out of consideration the probable active immunity indicated in a reported negative reaction to the Schick test.

PASSIVE TRANSFER AGAINST HORSE SERUM

The method known as passive transfer in common use in the study of human hypersensitiveness was employed to determine the possible presence of specific reagins for horse serum in the blood of the patient. This procedure, known also as the Prausnitz-Kustner[7] phenomenon, depends on the presence of these specific reacting substances in the blood of hypersensitive persons. When serum from such a subject is inoculated intracutaneously into a nonsensitive patient, these substances, or reagins, fix themselves locally in the subject into which they have been transferred, making him locally sensitive by passive transference of reagins. The site of inoculation thus rendered sensitive will react positively to the antigen for which the transferred reagins are specific, while a noninoculated site in the same subject remains unaffected (table 2).

Rabbits.—Passive transfer was performed by inoculating the patient's serum into rabbits (heterologous transfer) instead of human beings (homologous transfer) on account of the positive Wassermann reaction and the possibility of producing local necrosis if the transfer proved successful. It was striking that the mere injection of 0.2 cc. of the patient's serum caused such edema of the abdominal wall of the rabbit that the involved area, 20 by 30 cm., persisted a week. This result recalls the observation of Lewis,[8] in 1908, that the hypersensitive reaction to horse serum depends on the development of special antibodies that may be passively transferred to fresh animals. He noted that the animal into which serum has been transferred may even succumb to the test if the dose of hypersensitive serum is sufficiently intoxicating and given intravenously. An equal quantity of saline solution inoculated similarly into the same rabbit produced no reaction. Serums from the brother, the sister and a donor, a known syphilitic serum and antitoxin inoculated into rabbits produced no reaction. When the edema had subsided on the ninth day following the original injection, 0.2 cc. of diphtheria antitoxin was injected into the same site to determine whether any substance had been transferred in the patient's serum which would react with antitoxin. This would reflect the clinical process. Within fifteen minutes there were marked edema and reddening. In four hours the involvement covered an area 5 cm. in diameter, persisting for forty-eight hours and diminishing on the third day. A control injection into the site into which the saline solution had been inoculated produced no reaction in the rabbit. Furthermore, injections of antitoxin into the sites into which serum had been injected yielded no response in the sister and brother. The same procedure was followed in another rabbit that was inoculated with only 0.1 cc. of the

6. Schamberg, J. F., and Kolmer, J. A.: Acute Infectious Diseases, ed. 2, Philadelphia, Lea & Febiger, 1928.

7. Prausnitz, C., and Kustner, H.: Centralbl. f. Bakt. (Abt. 1) **86**:160 (April) 1921.

8. Lewis, P. A.: J. Exper. Med. **10**:1 (Jan.) 1908.

TABLE 2.—*Passive Transfer*

Serum.....	April 21, 1930	Reaction	April 30, 1930	15 Minutes (*Rabbit*)	4 Hours	May 7, 1930	4 Hours	24 Hours
Patient.....	Rabbit A 0.1 cc. intracutaneously o Saline control o	Edema, hyperemia 10 by 15 cm. until April 29, 1930 O O O O O	0.2 cc. of antitoxin intracutaneously in same site and saline control o	Beginning edema and hyperemia O O	Edema, hyperemia 10 cm. for 48 hours; decreasing 72 hours O O O O	0.2 cc. of donor's serum intracutaneously in same site and saline-antitoxin control o	Edema, slight hyperemia 3 cm. O O	Edema 7 by 10 cm.; necrosis 2 cm. O O O O
	Rabbit B 0.2 cc. intracutaneously o Saline control o	Similar reaction 20 by 30 cm. O O O O O O O O O O	o	O O	Same 5 cm. O O	0.2 cc. of donor's serum intracutaneously in same site and saline-antitoxin control o	Same 2 by 3 cm. O o	Edema 9 by 15 cm.; slight necrosis 1 by 1 cm. O O O O O
Sister.....	o	o	o	o	.....	.....	.....	.....
Brother.....	o	o	o	o	.....	.....	.....	.....
Antitoxin control..	.....	.....	o	o	.....	.....	.....	.....
Donor control.....	.....	.....	.....	.....	.....	o	.....	.....
Antitoxin Donor } Control	.....	.....	o	o	.....	o	.....	.....
Syphilitic Antitoxin } Control	0.2 cc. 4 plus serum o	o	o	o	.....	.....	.....	.....
Syphilitic Donor } Control	0.25 cc. 4 plus serum o	Slight pink edema 4 cm. O O	0.25 cc. of donor's serum o	o	o	.....	.....	.....
				(*Guinea-Pig*)				
Patient.....	o	Necrosis 1 by 2 cm. O o	o	Slight purple edema O O	Edema, hyperemia 4 by 4 cm. 48 hrs.; decreasing 72 hrs. O O			

* In this table and in table 3, the size and number of the circles indicate the comparative intensities of the reactions.

patient's serum in order to minimize the extensive reaction from the primary injection previously noted. However, the edema reappeared, this time involving a larger area, namely, 10 by 15 cm., and again it was necessary to wait a week before the reaction subsided. Antitoxin inoculated at the site of the injection of the patient's serum into this animal produced the same reaction as previously, except that the area of edema and hyperemia covered a larger surface, probably due to a variability of reaction in the two animals. The observations thus far indicated that the patient's serum contained some substance toxic to the rabbit's skin. This substance was absent in the serum of the sister, brother and donor, a known syphilitic serum and antitoxin itself. Furthermore, a substance was transferred from the patient's serum only which reacted with horse serum (diphtheria antitoxin). To prove that the syphilitic element did not enter into the reaction, a cutaneous site was inoculated with syphilitic serum without reaction. When antitoxin was superimposed on this site, no change occurred.

Guinea-Pig.—Passive transfer was repeated, a guinea-pig being used. By the seventh day there was a small area of necrosis from the serum alone. On the ninth day, 0.2 cc. of diphtheria antitoxin injected into the site caused a purple, slightly edematous area in less than thirty minutes. Within four hours there was an area of edema and hyperemia 4 cm. in diameter, which persisted forty-eight hours and diminished in seventy-two hours. The reaction of the serum alone resembled that produced in the rabbit with the exception of the slight area of necrosis. This lesion probably reduced the reactivity to antitoxin, although the evolution of the injection of antitoxin duplicated the condition in the rabbit.

PASSIVE TRANSFER AGAINST DONOR'S SERUM

To obtain data concerning the clinical condition that produced the death of the patient, donor's serum was superimposed on the site previously treated with the patient's serum and antitoxin. In four hours there were edema and slight reddening 3 cm. in diameter. In twenty-four hours the edema extended over an area 9 by 15 cm., and there was an area of slight necrosis 1 cm. in diameter. The same procedure, when repeated in the rabbit receiving only 1 cc. of patient's serum followed by antitoxin, produced a similar result. In four hours the zone of edema and hyperemia reached 2 by 3 cm., and in twenty-four hours the area was 7 by 10 cm., with an area of necrosis 2 cm. in diameter. The larger area of necrosis in the rabbit receiving the smaller amount of patient's serum coincides with the greater reaction to antitoxin on patient's serum which this animal manifested at the site of transfer of the patient's serum previously discussed. Controls with donor's serum on untreated rabbit's skin, donor's serum on antitoxin and donor's serum on type I (Jansky) syphilitic serum proved negative. These results indicate that the donor's serum exerts a toxic reaction to the patient's serum in its entirety without affecting its antitoxic or syphilitic content individually. The immunologic license for the multiple transfer of antitoxin and donor's serum on patient's serum is discussed later.

SHWARTZMAN PHENOMENON

We thought that it would be of interest to determine what reaction would occur following the technic of Shwartzman.[9] He found that injection of typhoid bacillus cultures filtrated into the skin sensitized the skin so that an intravenous injection of the same antigen within twenty-four hours resulted in a local response consist-

9. Shwartzman, Gregory: J. Exper. Med. **48**:247 (Aug.) 1928.

ing of a severe hemorrhagic reaction. Sometimes local necrosis occurred, and sometimes death. Shwartzman considered his phenomenon unlike anaphylaxis, the Arthus phenomenon or similar reactions (table 3).

A rabbit was given an intracutaneous injection of 0.2 cc. of the patient's serum. In twenty hours an edematous area appeared locally, 2 by 4 cm. in diameter, and the rabbit acted sick. Twenty-four hours after the first injection, 4.5 cc. of the patient's serum was injected intravenously, a dosage of 1.5 cc. per kilogram. Three hours later there was severe diarrhea, and in five hours the animal died with diffuse hemorrhage over the whole abdomen. The hemorrhage was more severe at the site of the original injection, and there was an area of necrosis 4 by 4 cm.

A second rabbit was similarly treated with 0.25 cm. of the patient's serum. Within twenty hours there was a blanched area about 1.5 cm. in diameter at the site of injection surrounded by an irregular purple halo from 1 to 2 cm. wide.

TABLE 3.—*Shwartzman Phenomenon (Rabbit)*

Serum	Intracutaneous	20 Hour Reaction	Intravenous	3 Hour Reaction	5 Hour Reaction
Patient.....	Rabbit A 0.2 cc. o	Rabbit ill; edema 2 by 4 cm.	4.5 cc., i.e., 1.5 cc. per kilogram	Severe diarrhea	Diffuse hemorrhage over entire abdomen more severe at site of injection; necrosis 4 by 4 cm.
	Rabbit B 0.25 cc. o	Blanched area 1.5 cm.; purple halo irregular 0.5 cm.	2.0 cc., i.e., 0.67 cc. per kilogram	Death	Death
Sister.....	Rabbit B 0.25 cc. o	Slight hemorrhage at site	2.0 cc., i.e., 1.5 cc. per kilogram	.....	.....
Brother.....	Rabbit B 0.25 cc. o	.....	2.0 cc., i.e., 1.5 cc. per kilogram	.....	.....
Positive syphilitic.	Rabbit B 0.25 cc. o	.....	2.0 cc., i.e., 1.5 cc. per kilogram	.....	.....
Donor.....	Rabbit B 0.25 cc.	.....	2.0 cc., i.e., 1.5 cc. per kilogram	.....	.....

This appearance significantly resembled one stage in the evolution of the lesion produced in the patient clinically on the second day of her reaction. When 2 cc. of the patient's serum, representing a dosage of 0.7 cc. per kilogram, was injected intravenously, the rabbit died in less than one hour.

A control injection of the sister's serum produced a slight hemorrhagic reaction at the site of intracutaneous injection, but subsequent intravenous injection of 1.5 cc. per kilogram of her serum provoked no local or general reaction. The same procedure, when carried out with the brother's and the donor's serum and a known syphilitic serum as controls, yielded negative results. The Shwartzman phenomenon demonstrated in a new way that there was some toxic substance in the patient's serum not related to the syphilitic factor.

COMMENT

Clinical Data.—From the clinical standpoint it is noteworthy that the lesion of the Arthus phenomenon followed the injection of antitoxin into a patient still manifesting signs of reaction from a previous

dose, an observation stressed by Gatewood and Baldridge. There was a record of a negative reaction to the Schick test following the injections of toxin-antitoxin, but the physician in charge followed the directions of the health department to immunize the contacts with diphtheria antitoxin. When a culture from the patient's throat was reported positive, a curative dose of 15,000 units was administered, although there were no definite findings of exudate, a nasal discharge or laryngeal symptoms. The factor of distant involvement, particularly around the joints, was present in the cases of Gatewood and Baldridge. There is a suggestive relationship of this finding to the arthritic picture of some cases of serum sickness. It is most probable that the organisms found in the gangrenous mass were secondary invaders.

Controls.—The fortunate parallel controls of the brother and sister and the implicated donor's serum, besides the controls of single factors, such as a known syphilitic serum of the same type, Jansky I, antitoxin (horse serum) and saline solution, impressively fixed the authenticity of the reactions and the resulting conclusions.

Precipitins.—The presence of precipitins to horse serum corroborates the fact that artificial sensitization had developed in the patient alone. This finding fits in with the subsequent happenings to the patient, which were absent in the sister and brother.

Toxic Effect of Patient's Serum on Rabbit's Skin.—The immediate reaction produced by an intracutaneous injection of the patient's serum into the rabbit's abdominal wall and the necrosis similarly produced in the guinea-pig's skin indicate that a specially elaborated antibody had been transferred, as Lewis claimed. The edema recalls an observation of Arthus and Breton,[10] that after five injections of horse serum into the abdominal cavity of the rabbit a subsequent injection into the abdominal wall causes a true edema without reddening in twenty-four hours. In our experiment it seems that this antibody or serologic end-product, the result of five previous intramuscular injections of horse serum into the patient, had been transferred, already elaborated, to the rabbit, with the production of the promised edema. It required only the addition of horse serum or diphtheria antitoxin locally, which was accomplished by passive transfer, to reproduce the clinical lesion. This immediate edematous response was not produced by any of the controls, again confirming that the establishment of the Arthus state was the essential process in the patient.

Reaction of Patient's Serum to Horse Serum by Heterologous Passive Transfer.—The reaction of the locally sensitized abdominal wall

10. Arthus, M. M., and Breton, Maurice: Compt. rend. Soc. de biol. **55**:1478 (Nov.) 1903.

of the rabbit to superimposed horse serum resembled strikingly the earlier stages of edema and hyperemia seen in the patient and reproduced the picture of milder response limited to hyperemia and edema described previously (see Addendum). It is probable that necrosis more definitely resembling the clinical picture might have occurred had the transfer been made intramuscularly instead of intracutaneously, because, it will be recalled, all of the patient's inoculations were made into the gluteal muscles. The factor of local hypersensitiveness looms large in this connection.

Reaction of Patient's Serum to Donor's Serum by Secondary Imposition.—The reaction of necrosis to further superimposition of donor's serum may indicate that there is some form of crisis produced by the interaction of these two serums despite their compatibility, which was checked by typing and cross-agglutination. Here may be material for speculation concerning reactions to transfusions in cases of compatibility demonstrated by ordinary methods.

The crucial test was lacking because there was insufficient patient's serum to test directly against donor's serum. Nevertheless, there is indirect evidence that the necrosis observed in the site successively inoculated with patient's serum, horse serum and donor's serum was a true reaction between patient's and donor's serum. The primary reaction between the patient's serum at the site into which injection was made and horse serum antitoxin had disappeared before donor's serum was added. Donor's serum in a control test produced no reaction on horse serum (diphtheria antitoxin). Therefore, if the intermediate horse serum is left out of consideration, there remains a true reaction of donor on patient. The syphilitic element of the patient may likewise be ignored by the negative results of another control test consisting of donor against a known syphilitic serum, type I, Jansky.

Of immunologic interest is the duration of passive sensitization of the rabbit by heterologous antibodies. Generally, this type of sensitivity lasts from six to ten days, which contrasts with homologous sensitization, which frequently persists for months.[11] Horse serum was injected into the sensitized site nine days after a transfer of the patient's serum, and donor's serum was superimposed sixteen days after the original transfer. This was seven days after horse serum had been injected, with a positive effect, and five days after the reaction to horse serum had subsided. On the basis both of time elapsed since heterologous transfer and of the fact that the tested site was not ideal for secondary testing after one previous positive reaction, even though the positive reaction was caused by an unrelated substance, horse serum, the authen-

11. Coca, A. F.; Walzer, Matthew, and Thommen, A. A.: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, 1931.

ticity of the patient-donor reaction may be questioned. However, it would appear that these orthodox objections would be pertinent if the reactions had been negative. In other words, the time factor can only prevent reaction, and a previous positive reaction tends to reduce local reactivity, though not necessarily. Finally, it is not too extravagant to conclude that there was a substance in the donor's serum which interacted with a substance in the patient's serum to produce a toxic action on the rabbit's skin. It would follow that the reaction of these two serums in the patient's circulation likewise produced a reaction that proved fatal to the patient.

Toxin Demonstrated by Shwartzman's Technic.—The Shwartzman phenomenon brought further proof to bear on the fact that some toxic substance had been elaborated in the serum of the patient alone which behaved like filtrates of typhoid bacilli. The rabbit tested by this technic died following the intravenous injection of patient's serum twenty-four hours after intracutaneous inoculation with the same material, and the local site reacted selectively. The blanched local site of inoculation surrounded by a purple halo strikingly resembled one stage in the clinical picture of the child.

Irrelevance of Syphilis.—The factor of syphilitic infection as a determining element was excluded serologically by controlling with a known syphilitic serum of the identical blood group in order to reproduce identical conditions. In addition, the sister served as a control from the standpoint of having a 3 plus Kahn reaction and four previous inoculations of antitoxin and toxin-antitoxin identical with the first four inoculations of the patient in point of time and lot of serum. The known syphilitic serum was inert in all its reactions on rabbit's skin and in its interactions with antitoxin and donor's serum.

SUMMARY

1. In a syphilitic patient with the Arthus phenomenon resulting from injections of horse serum (diphtheria antitoxin and toxin-antitoxin), precipitins to horse serum were demonstrated.

2. The patient's serum contained a transferable substance toxic for rabbit's and guinea-pig's skin.

3. This substance interacted with horse serum (diphtheria antitoxin) when passively transferred to a rabbit or a guinea-pig.

4. It was capable of further demonstration by the technic of Shwartzman.

5. The serum of the patient probably contained a transferable substance which produced a toxic interaction with donor's serum in the rabbit's skin.

6. Controls with essentially similar serums from members of the same family similarly treated but not manifesting the Arthus picture were negative.

7. The fatal reaction to transfusion, despite agglutinin and hemolysin compatibility, was due to other changes in the patient's blood incident to the Arthus phenomenon.

8. A search of the literature indicates that this is the first study of its kind.

CONCLUSIONS

1. The phenomenon described by Arthus may be reproduced in human beings.

2. Caution should be exercised in the administration of serum in the presence of reactions from previous injections of the same type, although necessary serum must not be withheld.

3. Reactions of this type will be more common when the large group of children immunized with the horse serum type of toxin-antitoxin in the last decade come into contact with other types of horse serum.

4. Although active immunization against diphtheria has been made possible in the last few years by the use of sheep and goat serum and more recently by the use of toxoid preparations free from serums, there still remain so many potentially sensitized children that therapeutic agents should be prepared in serum other than horse serum to be used by choice in this permanently susceptible generation.

5. The manifestation of the Arthus reaction may constitute a transfusion hazard.

ADDENDUM

Since this paper was prepared, one of us (Dr. Tumpeer) and his associate, Dr. A. Matheson, have had a nonsyphilitic patient under observation with a less severe form of the reaction than the one described herewith. In this child the lesion followed an injection of tetanus antitoxin three months after a previous similar injection and four years after the three weekly injections of horse serum toxin-antitoxin. Passive transfer was performed, the mother of the patient being used as the recipient, with a positive reaction to horse serum (tetanus antitoxin).

Dr. William Thalhimer, director of laboratories, and Dr. Katherine M. Howell, head of the department of bacteriology and serology, Michael Reese Hospital, helped us in this work.

Progress in Pediatrics

CONDITIONED REFLEXES IN PSYCHOPATHOLOGY OF CHILDHOOD

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The history of medicine shows that every important step in the progress of scientific medicine has been followed by development in the corresponding branch of clinical medicine. Among the biologic disciplines physiology is especially closely connected with the clinic. At the close of the last century the physiologists made great progress in the investigation of almost all organs, but physiologic study of the brain remained decidedly backward.

However, during the last three decades there have been great achievements in this branch of physiology. In 1901, Prof. I. P. Pavlov, with many co-workers, began an intensive study of the higher nervous activity in animals by the strictly physiologic method of conditioned reflexes. Great results have been attained in this field of investigation, and many important laws regulating cerebral activity have been discovered by these workers.

The inspiring advances of Pavlov's work stimulated me to elaborate on the method, so that it could be used for the strictly physiologic study of the activity of the brain in human beings. During many years of continuous work this aim has been attained. At present it can be truly said that the physiologic technic [1] is so far advanced that it is possible to investigate this physiologic activity of the brain in children under the same conditions and with no less exactness than it is done on animals in the physiologic laboratories of my great teacher.

For twenty-four years my associates and I have been collecting material concerning the activity of the brain, not only in normal, but also in psychopathologic, children. We endeavor to discover the physiologic nature of various pathologic conditions in order to establish a sound scientific basis for the advancement of practical methods which will improve the condition of the patient.

Until recently the scientific basis of psychopathology had to be sought in psychology, as the physiologic data were rather desultory and scanty; now knowledge exists of the physiology of the cerebral hemisphere, not only of animals but also of man. The great achievements of

1. Krasnogorski, N. I.: Bedingte und unbedingte Reflex im Kindesalter und ihre Bedeutung für die Klinik, Ergebn. d. inn. Med. u. Kinderh. **39**:613, 1931.

modern psychology in connection with the progress of cerebral physiology create conditions under which the most complete knowledge of the activity of normal and pathologic brains may be attained by the united efforts of psychologists, physiologists and physicians.

The cerebral hemispheres, being the highest part of the central nervous system, comprise the organ which realizes the most complex reflex activity. The reflexes of the spinal cord are relatively simple, but they become more complex according to their proximity to the brain and are most complex in the region immediately beneath the cerebral cortex.

The study of epidemic encephalitis contributed greatly to the knowledge of the physiologic function of the infracortical regions. These are the highest parts of the nervous system, where the most complex coordination of innate, unconditioned reflexes is accomplished. Probably such complex unconditioned activities as instincts, affects and simple emotions are chiefly localized here. A patient with extreme idiocy disposes of all the complex coordinations of the unconditioned reflexes; he shows instinctive, affective and emotional reactions, but he is a complete invalid. He cannot exist without the help of other people, for he is unable to adapt these inert, innate reflex activities to the ever-changing conditions of the outer world. This adjustment is realized in a normal person in the cortex of the cerebral hemispheres by means of the conditioned reflex mechanisms. The various stimulations always arising in the person's environment become conditioned and begin to evoke one or another activity if they have occurred simultaneously with this activity several times. The reflexes of the cerebral cortex are temporary, acquired, adaptive conditioned reactions which function as long as the conditions under which they have been established exist.[2]

Together with positive functions, the cerebral hemispheres develop an enormous inhibitory activity. The cortical inhibitory reactions show also all the characteristic features of conditioned reflexes. They are temporary, acquired, changeable reactions, representing the highest degree of adaptation. Cortical inhibition manifests itself in various forms. Extinction, differentiation and delaying of the conditioned reflexes and the formation of conditioned inhibitions, hypnotic states and sleep are different manifestations of the same nervous process of intracortical inhibition.

In 1911, working in Pavlov's laboratory on animals, I proved that the intracortical inhibition arising in any point of the cerebral hemispheres does not remain immobile, but radiates over the other parts of the cortex along definite pathways at a certain speed.

2. Every new external agent can be made negatively conditioned and becomes able to inhibit the positive reflex, if it is employed several times with the conditioned positive stimulus and their combined action left without reenforcement.

In the normal brain inhibition does not continue to irradiate, but begins gradually to concentrate at its starting points. At first it leaves the distant, and then the nearer, parts of the cortex from the inhibitory focus. Radiation and concentration are two fundamental principles of the dynamics of the cerebral hemispheres.

The third fundamental principle, discovered by Sherrington for spinal reflexes and by Pavlov for cerebral hemispheres, is reciprocal induction. It manifests itself in the fact that the excitation of some cortical cells produce inhibition in other cells—positive induction—and, reversely, inhibition inducts excitation—negative induction.

The correct interaction of radiation, concentration and induction ensures a flexible and mobile dynamic equilibrium among conditioned reflex systems in the cerebral cortex. The cortical reactivity does not remain constant even in normal children; its phasic fluctuations are of special interest in psychopathology.

Under conditions of optimal excitability the cortical cells respond to strong conditioned agencies by more intense reflex effects than if the stimuli are weak. However, as soon as optimal excitability has passed children begin to react in a different manner. Weak and strong stimuli produce the same reflex effect, either equally strong (leveling excitatory phase) or equally weak (leveling inhibitory phase), or weak stimuli even produce a greater effect than stronger stimuli (paradoxical phase). The ultraparadoxical phase, i. e., when positive stimuli elicit negative effects and inhibitory stimuli positive effects, is very important. In the hypnotic phase the cerebral hemispheres are in a state of inhibition, except restricted areas which remain in a waking state. Owing to radiation of inhibition, all the conditioned reflexes disappear, except the reflexes which are controlled by these areas. In normal children the phases are transient, but in those with pathologic conditions they acquire a permanent, stable character and form the basis of the symptoms.

TYPES OF IDIOCY

The most profound disorders of conditioned reflex activity are revealed in different forms of idiocy. In persons with the most severe cases of congenital idiocy the cortical functions are so deeply disturbed that even the establishment of conditioned reflexes is entirely impossible. These persons are incapable of developing the most elementary adaptive reactions; they are complete cerebral invalids. One deals with a state which can be truly termed as complete cortical areflexia.

To the second group belong patients who are able to realize a certain conditioned reflex activity; this activity, however, is abnormal. These children show some natural conditioned responses. Showing and bringing food to them evoke the conditioned motor and secretory

responses. But the extreme cortical insufficiency manifests itself as soon as one tries to establish the artificial conditioned reflexes. Hundreds of times the external stimulus would be applied at the same time that the child was given food without any conditioned connection being established. The excitability of the cortical cells is extremely low in these patients. It is proved by the fact that the conditioned reflexes could be established quickly if one applied a more intense reenforcement; e. g., stimulation by a weak electric current usually produced an intense defensive unconditioned reaction. Obviously, in these cases the usual excitation of the feeding center is not intense enough to increase the excitability of the cerebral hemispheres to the degree necessary for the establishment of the conditioned reflex arcs. As a contrast to the food reflex in idiots, the defensive motor reflexes decidedly dominate other reflexes, and on their basis the widely generalized conditioned reflexes can be formed which have the character of permanent reactions that cannot be abolished.

The tendency to generalization of the conditioned reflexes in idiots is based on abnormally wide radiation of an excitatory process. The sphere and character of radiation greatly depend on the resistance which arises in the form of countless positive and inhibitory conditioned reflex systems in the cerebral hemispheres. The more the cerebral cortex is differentiated and divided into areas controlling conditioned reflex systems, the more limited and expedient are the radiations. In the cerebral hemispheres of idiots these conditions are entirely lacking.

The complete insufficiency of cortical inhibition manifests itself in the deep disturbance of the analyzing activity of the hemispheres. The formation of differentiations is either impossible or difficult. In the latter case, only most primitive differentiations can be formed, but they are unstable and disappear quickly.

A characteristic feature of the second group of patients is the complete bankruptcy of the cortical inhibition. Under conditions in which normal children establish the inhibitory reflexes, idiots exhibit intense excitatory reflex effects.

The patients in the third group are on a low level in analyzing and synthetic work. The reactivity of the cerebral hemispheres is distinctly decreased. They are able to make the stimuli conditioned; they establish differentiations and other inhibitive reflexes, but all these reactions are different from those in the normal brain. The formation of reflexes is slow; the stability of the conditioned reflex arcs is markedly diminished, and the conditioned connections are easily erased by time. The cortical inhibitory reflex effects are weak and not easily inhibitable.

Characteristic for this group of children are the extensive periodic fluctuations of the cortical reactivity. The periods of more or less normal reactivity are often replaced by periods in which the conditioned reflexes decrease or disappear for several days or even weeks.

The slowness of formation and the instability of the conditioned reflex arcs cause the conditioned reflex systems to be poor and limited. Therefore, analytic and synthetic activities are on a low level.

In the normal brain the conditioned reflex systems are always in a state of mobile equilibrium. When this equilibrium is destroyed, they quickly reestablish a new equilibrium and begin to function as new dynamic systems. This flexibility of the dynamic balance is lacking in a deficient brain. As soon as the equilibrium of the system, or of the complex of systems, is disturbed, inhibition develops which may last a long time. The inertness of cortical inhibition is a characteristic feature of the cerebral activity in these patients.

The profound disorders of the physiologic activity of the brain found in idiocy represent, of course, an extreme degree of impairment of the basic neural mechanisms and dynamics of the cerebral cortex. The knowledge of the presence of these disturbances is important, as it enables one to understand better the facts obtained in studying other pathologic conditions.

On the other hand, if the etiologic factors remain the most important for classification of the different forms of idiocy, examination of the function of the basic cortical mechanisms by the conditioned reflex method makes possible an objective grading of the cortical insufficiency. Here the etiologic and physiologic principles supplement each other most successfully.

MYXEDEMA

Great and typical disturbances of the conditioned reflexes were found in children suffering from endocrine disorders, especially from myxedema. The insufficient production of thyroxin greatly influences not only cortical but also infracortical reflexes. The unconditioned secretory reflexes in myxedema are greatly decreased; the unconditioned motor reactions are also weak, slow and inert. This fact is in itself of great significance for the function of the cerebral hemispheres, as the infracortical activities form the basis on which the conditioned responses are built. A great decrease of excitability of the subcortical centers leads inevitably to the decrease of excitability of the corresponding cortical fields. The greater the endocrine disorder, the more impaired is the conditioned reflex activity. In severe, neglected cases of myxedema, the same characteristic changes of the cortical activity are found as are seen in congenital idiocy: slow establishment and decreased magnitude of reflexes, long latency and aftereffects of long duration. The curve of the conditioned motor response

is typical of myxedema. In normal children the curve rises rapidly after a short latent period, attains its maximum within the fraction of a second, and then remains on the same level as long as the stimulation lasts; in children with myxedema it rises slowly, reaching its maximum only after from seven to fourteen or more seconds. The refractory phase of the reflexes is also much longer in patients with myxedema than in normal children.

Thus an insufficient supply of thyroxin in the organism leads to great impairment of the function of the associative mechanism of the cortex. The patient suffering from myxedema cannot quickly make those subtle adaptations to the ever-changing environmental conditions which a normal child does by formation of new conditioned responses.

The inhibitory functions of the cerebral hemispheres are deeply disturbed. For instance, the abolished conditioned reflexes are reestablished in patients with myxedema much more slowly than in normal children. The excitability of the conditioned reflex arc, decreased as a result of the abolished reflexes, is reestablished slowly after a number of reenforcements. Obviously, the production of the nervous energy necessary for the restoration of the former excitability is markedly diminished in patients with myxedema.

In severe cases the mechanism of conditioned inhibition has been found to be very much disturbed. In some patients an attempt to form a conditioned inhibition produces a general decrease of the cortical excitability and a shifting of the dynamic equilibrium toward inhibition of long duration. In other cases, instead of inhibitory reflexes positive reflex effects of the second and third orders appear, i. e., a symptom characteristic of extreme idiocy.

Great disturbances were observed in differentiating functions of the cerebral hemispheres. In patients with severe myxedema, even the most simple differentiation, e. g., between two places on the skin 12 cm. apart, could not be established.

An intense successive inhibition which develops after application of inhibitory stimulations is characteristic in myxedema. In severe cases one inhibitory stimulation was often sufficient to inhibit the following conditioned reflexes so intensively that they could not be reestablished up to the end of the experiment.

Thus the negative stimulation produces in the corresponding cortical cells an inhibitory process which radiates over the cerebral hemispheres and inhibits the cortical reflexes. On the other hand, concentration of inhibition and positive induction are pathologically decreased; the reestablishment of cortical excitability proceeds slowly. This fact must be attributed to the specific chemical changes in the nerve cells in myxedema. Owing to the pathologic metabolic conditions, the cortical cells are unable to reestablish quickly the potential

of nervous energy necessary for the conditioned reaction. Insufficient production of thyroxin leads not only to the quantitative, but also to the deep qualitative, disturbances of the activity of the cerebral hemispheres.

Treatment with thyroidin showed a favorable effect on the conditioned reflex activity in all of our cases. It raised not only cortical, but also infracortical, excitability, increasing both conditioned and unconditioned reflex effects. If before treatment the conditioned salivary reflexes were producing only two or three drops of saliva, they increased usually so that there were six to eight drops after treatment. The character of the curve of the motor reflexes also approached the norm. In charts 1 and 2 are shown the conditioned motor reflex before and after nine months of treatment.

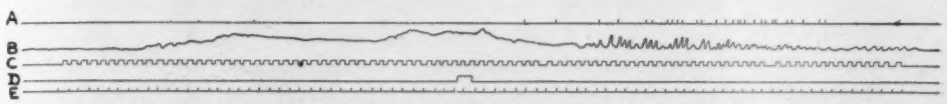


Chart 1.—Conditioned and unconditioned reflexes in myxedema before the treatment with thyroidin. *A* represents the salivary secretion; *B*, the motor reflex; *C*, skin stimulation; *D*, food, and *E*, time.

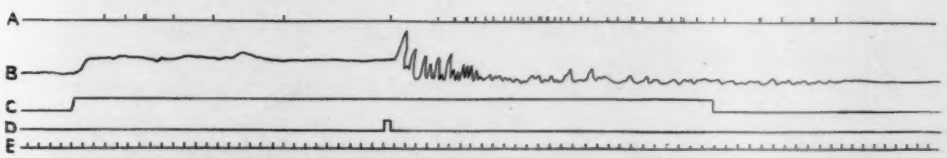


Chart 2.—Conditioned and unconditioned reflexes in myxedema after nine months' treatment with thyroidin. *A* represents the salivary secretion; *B*, the motor reflex; *C*, metronome; *D*, food, and *E*, time.

Thyroidin produces a favorable effect on cortical inhibition. After several months of treatment the establishment of inhibitory reflexes, e. g., conditioned inhibitions and differentiations, becomes possible in most cases. The successive inhibition loses its inertness and begins to concentrate quicker. Thyroidin considerably intensifies positive induction, which is so weak in these patients. The great improvement in the qualitative disturbances of the cortical activity proves that thyroxin acts directly on the cortical cells, increasing their excitability and apparently producing a more or less normal metabolism. It seems that thyroidin helps the cortical cells to increase considerably the production of nervous energy. This assumption would explain why thyroidin helps the cortical cells to free themselves more quickly from various inhibitory states, which are so deep and last so long in cases of untreated myxedema.

RICKETS

Of special pediatric interest is the investigation of the physiologic activity of the brain in children suffering from rickets. The changes in the psychic life of these patients have always attracted the attention of physicians, but simple clinical observation was obviously not sufficient to obtain satisfactory data.

In 1913 it could be shown that conditioned reflex activity is considerably disturbed in rickets. The establishment of conditioned responses proceeds very slowly; e. g., they are produced after one hundred and fifty or more trials. The conditioned reflexes are unstable and disappear periodically, sometimes, for several days. The motor reflexes have a characteristically long latency, three or four seconds, which becomes shorter only after prolonged training. The orienting reflex is greatly decreased in these children, and they react only slightly to new stimulations in their environment. Patients with rickets cannot resist the monotony of the experimental conditions and are soon in inhibitory states.

It is interesting to note that in cases in which there is extensive rachitic myotonia, the conditioned reflexes following impulses originating in muscles are established with greater difficulty than following stimulations from other analysors. It seems that in the period of disturbance of the statical functions the reactivity of the motor analysor is especially impaired.

The inhibitory function of the cerebral hemispheres is also greatly disturbed in rickets. The abolishing of reflexes in rachitic patients, as in idiots, is slow, the reactivation being retarded. Inhibition radiates widely over the cortex and remains a long time; its concentration is markedly lowered.

The foregoing facts show that the reactivity of the cortical cells is considerably decreased in rickets. New external agencies do not elicit the subtle adaptive responses which are accomplished so quickly and on such a large scale by the normal brain.

Thus the disturbance of the conditioned reflexes in rickets has many features similar to disorders observed in idiocy and myxedema. However, the cortical functions in rickets are much less impaired than in the other conditions. The cortical disturbances in rickets are not permanent, and as soon as the general condition of the patient improves they gradually diminish and at last disappear entirely.

To determine how far these disturbances may influence the development of the brain in later years requires further investigation.

The study of the cortical reaction in rickets shows what a close connection exists between the general chemical make-up of the organism and the physiologic activity of the brain. The abnormal metabolic con-

ditions in the rachitic organism are those which decrease the excitability of the cortical cells and lead to impaired function in the cerebral hemispheres.

EPILEPSY

The conditioned reflex technic found wide application in research on epilepsy. By this method it was possible to investigate physiologically all changes in the cerebral activity in the period free from attacks as well as during and after convulsions. There arose many important questions: What is the state of the cerebral cortex during convulsions? What is the influence of the fit on the cortical and subcortical reactivity? What significance have the intensity, frequency and duration of the fits and the type of nervous system?

It was soon found that a single convulsion of short duration does not usually produce greatly deleterious effects on the conditioned reflexes. On the contrary, intense, frequent convulsions of long duration produce a profound and permanent disorder, not only of the cortical, but also of the infracortical, activities.

The influence of an epileptic fit on the conditioned and unconditioned reflexes was observed in a 13 year old girl; the results are presented in table 1. The convulsions set in at the moment when the conditioned stimulation (metronome) was in action and the child was eating sweetened cranberries. The fit stopped abruptly the secretion which was just beginning in response to the unconditioned reflexes. Notwithstanding that the child's mouth was full of acid berries, there was not a drop of saliva. The convulsion lasted two minutes, and as soon as it was over the child was stimulated again by means of the metronome and was given cranberries. However, there were responses neither to the conditioned nor to the unconditioned reflexes. The extreme excitation of the motor infracortical centers during the convulsion had entirely inhibited the motor and secretory cortical reflexes. The inhibitions disappeared rather quickly this time; the conditioned motor reflex became reestablished five minutes after the fit and the conditioned secretion after twenty minutes.

In this experiment the conditioned reflexes were obtained immediately before the fit. A different result was obtained from the same patient when her condition grew worse; the fits became more intense and appeared in series. In chart 3 is shown a progressive decrease of conditioned and unconditioned secretory reflexes in this child as early as two days before the series of six successive fits.

The same fact was noticed with regard to the reestablishment of the cortical functions after convulsions. After a single and comparatively mild convulsion the conditioned reflex activity was restored, sometimes within several minutes. However, as soon at the fits became

more frequent and intense, their deleterious after-effect increased immensely. The same chart shows that after the series of fits the conditioned reflexes were deeply inhibited and decreased during four days and the unconditioned reflexes, during two days. Thus attacks of grand mal undoubtedly produced a deleterious effect on the cerebral hemispheres.

In the period following convulsions the most varied inhibitory phases were often observed, which gradually replaced one another. The hypnotic, ultraparadoxical, paradoxical, narcotic, leveling inhibitory phases followed one another until normal reactivity was restored. In table 2 are presented the responses during an ultraparadoxical phase, which lasted for five days; during this time all the positive conditioned stimuli (red light, whistle and metronome) did not produce any conditioned responses, whereas the inhibitory agents, e. g., stimulation of the skin,

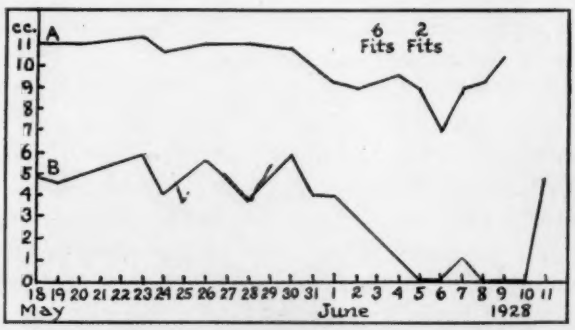


Chart 3.—*A* represents the unconditioned salivation following the ingestion of 20 Gm. of cranberries; *B*, the conditioned salivation in drops.

which had entirely inhibited conditioned metronome reflexes before the fit, now produced an intense conditioned reflex resulting on the average in from five to nine drops of saliva. On the fifth day after the convulsions the ultraparadoxical phase developed into the paradoxical phase, which gradually disappeared after the patient had begun to receive a ketogenic diet.

The results obtained by the study of the conditioned and unconditioned reflexes in epilepsy prove that during an epileptic fit the cerebral cortex is in a state of profound and complete inhibition. The inhibitory symptoms are sometimes observed several days before convulsions. Obviously the excitation which is increasing and concentrating in the cortical and infracortical motor centers up to the time of the fit inducts inhibition in other antagonistic centers. Therefore, the secretory reflexes become more and more inhibited. When the excitation of the motor cells attains its highest point, it is discharged in a general radiation of an intense excitation throughout the entire motor nervous system and

convulsions of the whole skeletal musculature are produced. This extreme excitation of the motor centers, as it were a motor storm, evokes profound inhibition radiating over the whole cortex and other infracortical centers. When all the conditioned and unconditioned

TABLE 1.—*Influence of an Epileptic Fit on the Unconditioned and Conditioned Reflexes in a Girl, Aged 13 Years*

Date	Time, Min.	Number of Stimuli	Stimuli	Conditioned Secretory Reflex, Drops per 30 Sec.	Conditioned Motor Reflex	Latent Period of the Motor Reflex, Sec.	Conditioned Salivation, Cc.	Comments
12/3/28	...	678	Metronome*	13	+	1.2	Some drops; no secretion	Food convulsions
			The fit lasted 2 minutes					
	2	679	Metronome	0	0	...	0	Food
	2	680	Metronome	0	Traces	17.0	0	Food
	3	681	Metronome	0	+	3.8	0	Food
	8	682	Metronome	0	+	1.2	4.5	Food
	2	683	Metronome	3	0	...	7.0	Food
	3	684	Metronome	5	+	1.6	8.0	Food
	3	685	Metronome	8	+	1.6	8.0	Food

* The metronome is the positive conditioned stimulus evoking the positive motor and secretory reflexes.

TABLE 2.—*Ultraparadoxical Phase After Convulsions with Laudine T.*

Number of Experiment	Date, 1928	Number of Stimuli	Stimulation*	Conditioned Salivary Reflex in Drops During 30 Sec.	Latent Time, Sec.	Unconditioned Secretory Reflexes, Cc.	Comments
			Intense epileptic fits				
1	5/6	99	Whistle	0	..	8.8	Food
		199	Red light	0	..	...	Food
		1,097	Metronome	0	..	...	Food
		130	Metronome-skin stimuli	6	3	...	No food
		100	Whistle	1	8	...	Food
	8/6	105	Whistle	0	..	9.2	Food
		207	Red light	0	..	...	Food
		1,100	Metronome	0	..	...	Food
		133	Metronome-skin stimuli	5	12	...	No food
		106	Whistle	0	..	...	Food
	9/6	107	Whistle	1	10	10.7	Food
		210	Red light	0	..	...	Food
		1,100	Metronome	0	..	...	Food
		134	Metronome-skin stimuli	9	6	...	No food
		108	Whistle	0	..	...	Food
	10/6	109	Whistle	0			
		213	Red light	1	20	...	Food
		1,102	Metronome	0	..	...	Food
		135	Metronome-skin stimuli	9	4	...	No food
		110	Whistle	0	..	...	Food

* The whistle, metronome and red light are the positive conditioned stimuli. The cutaneous stimulation is the negative stimulus, inhibiting the metronome reflex.

secretory reflexes are completely inhibited, the whole analytic and synthetic work of the cortex is stopped.

There is no doubt that convulsions may be produced by the cortical excitations arising in the motor zone, i. e., in the motor analysor of the cortex. However, as soon as the motor storm develops in the extra-

cortical nervous system, the function of the whole cortex instantly becomes inhibited. The extremely sensitive and reactive elements of the cortex are joined into the most complex conditioned reflex systems, and complexes of systems can save themselves from this raging storm only by a rapid decrease of their excitability, by the development of an intense and widely radiating inhibition. From this point of view the general radiation of inhibition over the whole cortex during an epileptic fit must be considered as a highly important defensive act. Obviously, the loss of consciousness and the following sleep are the results of this general radiation of inhibition.

The fact that during an epileptic attack inhibition occurs in the cerebral cortex as a whole is verified by further changes in the cerebral activity which are observed after convulsions. All the inhibitory phases develop gradually, from the most profound to the less intense inhibitions. Single fits of short duration usually do not produce a considerable deleterious after-effect; on the contrary, intense, frequent convulsions of long duration produce a profound and lasting disturbance not only of the conditioned, but also of the unconditioned, reflex activity.

Thus the gradual decrease of the cortical reflexes in the period before convulsions, the complete disappearance of reflexes during convulsions and the gradual reestablishment of cortical reactivity after convulsions prove that the function of the cerebral cortex is deeply inhibited during an epileptic fit. During convulsions the inhibition extends also to the infracortical centers antagonistic to the motor centers, e. g., secretory centers, and decreases their activity.

The conditioned reflex method made it possible to follow objectively the results of different methods of treatment of epilepsy. There was quick disappearance of the extreme inhibitory phases of long duration when the ketogenic diet was used. Marked improvement in the conditioned reflexes was observed after phenobarbital and large doses of bromides and calcium were given.

FUNCTIONAL NEUROSES

The physiologic method opens an unlimited field for the investigation of functional neuroses. By means of conditioned reactions it is possible to reveal the pathologic changes in the reactivity not only of the cerebral cortex as a whole, but also of its separate conditioned reflex systems.

In the extensive investigation by my co-workers and me the cerebral activity in such a complex neurosis as hysteria was studied. Concerning the biologic nature of the polymorphic and changing manifestations of this typical functional disorder of the nerves there is not sufficient knowledge.

The study of the conditioned and unconditioned reflexes in hysteria allows one to suppose that one is dealing with a dynamic disorder of cortical and infracortical activities, based on the functional insufficiency of the cortical cells. The cerebral cells in hysterical persons are characterized by hypo-excitability and quick exhaustion. In severe cases one finds even the most elementary functions of the cerebral hemispheres disturbed: The cortical reflexes are established slowly, and their magnitude and specificity are decreased. In favorable cases the cortical responses sometimes do not show marked deviation from the normal standards. The more delicate pathologic changes of the cortical reactivity may usually be disclosed by the conditioned reflex method.

In most of the hysterical patients we observed an extreme sensitiveness of the cortical processes to new stimuli. As soon as some new stimulus began to act, the conditioned positive responses disappeared and the inhibitory reflexes did not inhibit.

One of the characteristic features is instability and extreme fluctuation of conditioned effects. The cortical cells in hysterical persons cannot tolerate an intense stimulation of long duration. More or less frequent repetition of a stimulus or prolongation of it produces a rapid decrease in and even disappearance of the conditioned reflex.

Another typical condition in the dynamics of the cerebral processes in hysterical persons must be emphasized, i. e., the tendency to wide radiation of intracortical inhibition. Inhibitory stimulations produce intense inhibitions radiating widely over the cortex. Every more or less difficult task requiring a certain strain on the inhibitory process in these patients leads to general decrease of the cortical reactivity and to development of hypnotic states of long duration.

The normal activity of the cerebral hemispheres is based on a precise and flexible balance between the excitatory and inhibitory processes. Excitation and inhibition easily replace one another, and the dynamic equilibrium, being disturbed, reestablishes itself quickly. In a hysterical child this flexibility of the balance is lacking; the dynamic equilibrium, being shifted aside, is not quickly restored, but results in excitatory or inhibitory after-effects of long duration.

The conflicts between excitation and inhibition are of the greatest significance in provoking symptoms of hysteria. If in the normal brain dynamic disorders arising from conflicts quickly disappear, in hysterical patients they produce deep depressions or intense excitations which sometimes distress the patient for a long time.

The most characteristic state of the cortical reactivity in hysteria is the paradoxical phase, in which strong stimuli produce either very small or no responses and weak stimuli elicit more intense conditioned reflex effects.

The paradoxical reactivity explains the symptom of suggestibility which is so characteristic of the clinical picture of this neurosis. The experiments of Dr. N. R. Shastin have shown that in normal children direct stimulations of the receptive organs (ears, eyes, etc.) always overcome the verbal stimulations which contradict them. For instance, if a normal child is stimulated simultaneously by a red light, which was made conditioned, and by the sentence "there is no red light," the child always responds by the positive reflex. Another type of reaction is seen in hysterical patients exhibiting a paradoxical reactivity. Weak verbal stimuli conquer the stronger, direct-acting stimuli from the outer world. This pathologic reactivity of the cerebral hemispheres has innumerable consequences. The surrounding reality can be distorted at every moment by verbal stimuli. The associative stimulations decidedly dominate the facts and determine the behavior of the patient. The normal critical ability based on the repeated relation of the real facts is considerably decreased.

The study of the cortical reflex activity under conditions of "suggestion" helps one to understand better two other fundamental symptoms of hysteria, i. e., anesthesia and paralysis.

How would the cortical reflexes change under the influence of suggested anesthesia? The experiments of Dr. N. N. Derevtshekova have shown that on parts of the skin where complete hemianesthesia was produced by verbal stimulation all the conditioned cutaneous reflexes disappeared on the anesthetized half of the body, while they were normal on the other side. Obviously the skin analysor of the anesthetized side was in a state of static inhibition, while that of the opposite side as well as other analysors could receive stimulation.

Another important observation was made. It was proved that if, during the stimulation of the anesthetized skin, other conditioned stimuli, even from other analysors, were tested, they did not elicit any positive effect; i. e., they were inhibited. Obviously under the influence of stimulation of the anesthetized skin the inhibition was intensified to such a degree that it lost its static character and spread over other analysors, stopping their conditioned reflexes.

Thus hysterical anesthesia is based on a temporary inactivation of the corresponding cortical areas by static inhibition. In these cases sometimes large cortical fields are inactivated and excluded from the general analysis and synthesis of the brain. This segregation of the cortex by stable static processes represents the most important symptom of hysteria.

The tendency to segregation of the cortex is the condition, which explains many clinical manifestations of this neurosis.

From our experiences with hypnosis in normal children we know that during a hypnotic trance various conditioned reflexes can be estab-

lished in the waking fields of the segregated cortex without being introduced into the general synthesis of the cortex. In a hypnotic trance the child can accomplish the most varied conditioned reactions without being aware of them (S. L. Levin). The same conditions exist in the cerebral cortex segregated by the static processes in hysterical patients. The stable conditioned connections may be formed here in the waking areas, but the reactions arising in them act as segregated processes, remaining out of the consciousness of the personal self. The patients perform the conditioned reflex acts without knowing why they do so. Obviously, owing to the tendency to segregation of the cortex, the co-conscious processes acquire an extraordinary wide sphere of action in hysterical persons.

Thus from a physiologic point of view hysteria is an inhibitory cortical neurosis, the characteristic features of which are easy exhaustibility of the cortical cells, loss of the normal flexibility of the dynamic balance, paradoxical reactivity and a tendency to wide radiations of inhibition and to the development of stable static processes, leading to segregations of the functions of the cerebral hemispheres for a long time.

Physiologic investigation disclosing the biologic nature of the fundamental symptoms of hysteria reveals its rational prophylaxis and treatment.

As hysteria is an inhibitory neurosis, it is advisable to avoid all the conditions which decrease the excitability of the cerebral hemispheres. To these belong all the fatiguing and exhausting factors. The cerebral cortex in hysterical patients cannot accomplish the tasks which are not difficult for the normal brain. Intense as well as monotonous stimulations must be avoided, as they produce different hypnotic states of long duration.

The extreme sensitiveness to extraneous stimuli, the exaggerated orientation reflex and decreased concentration necessitate the creation of special favorable conditions for successful educational work with hysterical children.

The most important factor in prophylaxis and treatment of hysteria is the strict control of stimuli. The exhaustible cortical cells cannot tolerate stimuli which are easily endured by a normal cortex.

As was just mentioned, the cerebral hemispheres in hysterical persons typically exhibit paradoxical reactivity when weak agencies elicit the optimal reflex effects. Therefore, weak stimuli are indicated as a special method of treatment. On the contrary, intense stimulation must be carefully avoided as strong stimuli aggravate the symptoms of hysteria. Thus the chief principle in treatment of hysteria is the creation of an environment in which all stimulation would correspond to the decreased reactivity of the cortical cells in these patients.

It is important to protect the child from intense conflicts between excitatory and inhibitory processes. As the chief cause of conflict is difficult inhibition of certain intense conditioned and unconditioned activities, all inhibitory tasks for the hysterical patient must correspond to the decreased ability of the cortex to develop inhibitory effects.

Treatment of the segregated states of the cortex is an important medical problem. By carefully taking the history of the patient, the physician can discover the conditioned reflex systems in the patient's subconsciousness and make them conscious by the formation of many new conditioned connections between these systems and the whole cortex. Having introduced the isolated systems into the general work of the brain, it is possible for the physician to establish a great number of special inhibitions by the method of conditioned reflexes and thereby attain the therapeutic effect.

CONCLUSIONS

Physiologic investigation of cerebral activity finds wide application in the clinic. It helps to reveal many important facts concerning all the fundamental functions of the pathologic brain and to establish true criteria for the estimation of the degree of impairment. It makes possible the disclosure of the biologic nature of many psychopathologic conditions and offers fundamental principles for their rational prophylaxis and treatment. I am convinced that the physiologic method will bring the same fruitful results in psychopathology as it has produced in all other domains of clinical science.

Pediatrics in Art

INFANTILE OBESITY

JOHN RUHRÄH, M.D.
BALTIMORE

Lorenzi di Credi (1453-about 1535), the Tuscan painter, fellow student of Leonardi da Vinci under Andreas Verocchio, painted many Madonnas and Holy Families. One of the latter in the Dresden Picture

The Virgin, the Christ Child and John

Gallery shows a good example of infantile obesity. The increased number of folds in the skin due to the fat underneath are particularly well done. It may be noted that although according to Holy Writ the Christ Child was circumcised on the eighth day there is no evidence of it. This is common to all the pictures of the infant Jesus. In one of the galleries in Venice I thought from a photograph that this was not the case, but an inspection of the painting showed it followed the rule. And still the modernists complain of the photographic quality of the older painting!

Pediatric Biographies

GIOVANNI FILIPPO INGRASSIAS
1510-1580

JOHN RUHRÄH, M.D.
BALTIMORE

Ingrassias is supposed to have been born in Recabuto near Palermo. He studied medicine at Padua, and received his doctorate in 1537. His ability gained for him an enviable reputation, and he was called to the chair of medicine in Naples. There his lectures on medicine and anatomy were soon attended by crowds of students, and his skill in practice gained for him the title of the Sicilian Hippocrates. In 1560, he left Naples and returned to Palermo, and three years later Philip II, King of Spain, made him physician in chief to Sicily and the adjacent islands. When the plague ravaged the countryside, he rendered great service and was granted a pension, which he refused to accept, an action so unusual that it was recorded in the accounts of his life.

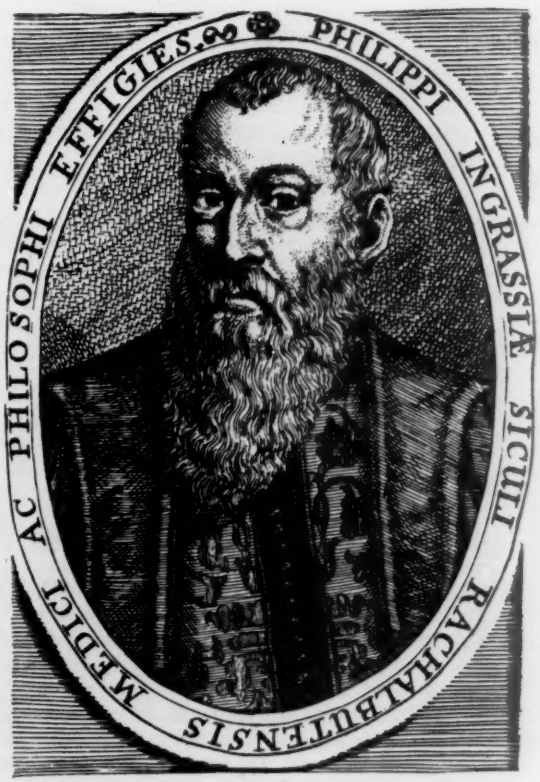
His name has been given by anatomists to the small wings of the sphenoid bone, which Geoffrey Saint-Hilaire called the ingrassian bone, although his description, it is said, is scarcely better than that of Galen. His descriptions of the bones are very good, and he is generally credited as the first to describe the stirrup of the auricular ossicles. He wrote on many topics, tumors, purgation by drugs, plague and infectious diseases, and also on questions relating to the reform of medical practice and medical legislation.

He is doubtless the first to describe scarlet fever clearly, and his description has been much quoted. He gave at the same time a short but clear description of chickenpox.

On page 194 of Ingrassias' "De tumoribus praeter naturam tomus primus," in considering smallpox and measles and allied diseases, he said:

> Moreover measles [which indeed the translator of Rhazes calls *blaccias*] purges mixed bile blood or mucus. Besides both these kinds I have seen everywhere, one of which is commonly called Rossaniam or Rossaliam, the other *crystallos* [chickenpox] which since, as is known, reddish pustules break out and are

dispersed over the whole body, the size of a pea, more or less, white and of a shiny crystal appearance which when they are opened one sees an aqueous fluid escape. The other indeed, is called *rossaniam* because there are dispersed over the entire body spots very large and small, fiery and red, scarcely raised sufficient to be worthy of mention; the appearance distinct from erysipelas, so that the whole body appears as if on fire [red hot]. Hence the common people think this to be of a kind with smallpox and measles. . . .



Giovanni Filippo Ingrassias

Ingrassias went on to quote some authorities on the subject of measles and smallpox and to comment on them.

We do not find Rossaniam described by them [the Arabians] unless we include it under Alhamika as I suppose must be taken for granted. . . . However, there are many people that think measles are the same as Rossalia but we have often seen with our own eyes that they are different, not trusting to the statement of other people.

News and Comment

UNIVERSITY NEWS

Dr. William H. Park, director of laboratories for the New York City Department of Health, has been appointed to the Hermann M. Biggs professorship of preventive medicine at New York University and Bellevue Hospital Medical College. This professorship was made possible by a memorial fund established shortly after the death of Dr. Biggs in 1923 and recently increased to a total amount of $200,000 by a bequest of Mrs. Hermann M. Biggs and gifts from William R. Biggs and Mrs. Katherine Biggs McKinney, son and daughter of Dr. Biggs, and by the Milbank Memorial Fund.

PERSONAL

Dr. Béla Schick has been given the annual gold medal awarded by Phi Lambda Kappa in recognition of his work on diphtheria.

GENERAL

Third International Pediatric Congress.—Americans wishing to contribute papers to the Third International Pediatric Congress to be held in London on July 20, 21 and 22, 1933, must give the titles of their papers to Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn., not later than March 15.

UNIVERSITY NEWS

Dr. Alfred F. Hess, New York, will give the Ingleby Lectures at the University of Birmingham in the summer term of 1933.

Abstracts from Current Literature

Anatomy and Physiology

EMBRYONIC EPITHELIAL RESTS IN THE PITUITARY. WILLIAM SUSMAN, Brit. J. Surg. **19**:571 (April) 1932.

In this series there were 230 hypophyses examined. They were removed post mortem from persons in whom there were no recognizable pituitary symptoms before death. Seven per cent of the subjects were children from 1 to 9 years of age. Of the 230 hypophyses examined, 71 contained epithelial rests of an embryonic nature, the commonest being that of a squamous type. The article also contains a discussion of the embryology of the pituitary gland.

SUMMERFELDT, Toronto, Canada.

THE MEASUREMENTS OF THE THORAX AND ABDOMEN IN INFANCY. I. HILMI, Monatschr. f. Kinderh. **53**:250, 1932.

The writer introduces three sets of measurements: from the manubrium to the xiphoid process (M-x), from the xiphoid to the navel (x-0) and from the navel to the symphysis pubis (0-P).

Individual measurements are unimportant unless considered in relation to each other. In the normal child the total abdominal length is 1.7 times that of the thorax, while in the sick child it may be 3.5. A diminution in the relation of thorax to abdomen is abnormal. Again, normally the abdominal length is approximately one fourth of the total body length, while in the sick child it may increase to one third.

GERSTLEY, Chicago.

Pathology, Bacteriology and Biochemistry

ACTION OF THE PARATHYROID HORMONE ON THE EPIPHYSEAL JUNCTION OF THE YOUNG RAT. HANS SELYE, Arch. Path. **14**:60 (July) 1932.

Ten day old rats were inoculated with large doses of parathyroid hormone. The bones showed marked decalcification and delayed ossification, with broadening and irregularity of the epiphyseal cartilage and bending of the bones at the epiphyses. The changes were suggestive of severe rickets. Fibrous metaplasia of the bone marrow was seen at the points of bending where severe mechanical strain occurred. The author suggests a similar mechanism in the causation of osteitis fibrosa.

LEMASTER, Evanston, Ill.

THE CURATIVE EFFECTS OF CEREALS AND BISCUITS ON EXPERIMENTAL ANEMIAS. PEARL SUMMERFELDT, FREDERICK F. TISDALL and ALAN BROWN, Canad. M. A. J. **26**:666 (June) 1932.

In rats placed on an exclusive milk diet after weaning a secondary anemia of the nutritional type developed in from five to eight weeks. In these rats the hemoglobin is reduced to from 4 to 6 Gm. per hundred cubic centimeters of blood instead of the normal value at this age of from 13 to 15 Gm.

Anemia could be cured when from 33 to 50 per cent of the total diet consisted of a special cereal or a special biscuit in which there was a relatively high proportion of copper and iron. Other foods tested were farina, oatmeal, zwieback, arrow root and whole wheat biscuits. These did not cure the anemia when fed in the same proportions.

When a group of normal children were fed the special cereal there was an increase in hemoglobin, where with ordinary cereal there was no increase.

MOORE, Omaha.

THE GENESIS OF BLOOD PLATELETS. C. H. WATSON, Edinburgh M. J. **39**: 229 (April); 311 (May) 1932.

Among hematologists there is a growing dissatisfaction with the character of the knowledge regarding the blood platelet. The megakaryocytic theory of Wright (1906 to 1910) is still in about the same state as when it was first offered, having been neither further confirmed nor refuted. The theory itself has not been correlated with any clinical manifestations.

The author has arrived at the opinion that the platelet is a disintegration-product of the red blood cell. He first describes the platelet; then he attempts to produce in the fluid in which a count is made in the laboratory a type of disintegration of the red cells such as is frequently seen in the clinic. He offers an experimental procedure to demonstrate the relationship between the fluctuation of platelets and the destruction of red cells. He then reports a study of the damaged red cell with reference to its disappearance from the circulation and also a study of the origin of the blood platelet.

The author's presentation consumes forty-four pages of the April and May numbers of the Edinburgh periodical. The work was done under a grant from the Earl of Maray Trust Fund. It had the assistance of various departments of the University of Edinburgh. Because of its extensiveness and technical nature the original paper should be consulted by the reader who is interested.

NEFF, Kansas City, Mo.

GROWTH UNDER VITA GLASS. IAN N. SUTHERLAND, J. Hygiene **32**:211 (April) 1932.

An attempt to determine the value of vita glass was made in 60 young experimental rats over a period of 245 days. All were kept on the stock Sherman B diet.

A distinction between those kept under vita glass and those under ordinary glass could not be seen. The offspring of the latter rats grew at a normal rate.

Exposure was made with both the sun's rays and a quartz mercury vapor lamp as a source. In both instances growth was the same as under ordinary glass.

JANNEY, Milwaukee.

ACTION OF INTRAVENOUS INJECTIONS OF SODIUM OXALATE ON CALCEMIA IN THE RABBITT. A. CHOAY and S. RENNES, Presse méd. **40**:697 (April 30) 1932.

Experiments to determine the effect of intravenous injections of sodium oxalate on the blood calcium of the rabbit showed that doses of 20 mg. caused the calcium to fall to zero, and the animal died with contractures, opisthotonos and laryngospasm. Smaller doses (100 mg.) caused a moderate drop in calcium, and some compensatory mechanism caused a return to the original figure.

BIEKER, St. Petersburg, Fla.

CHANGES IN THE SPINAL FLUID IN EXPERIMENTAL PAROTITIS. M. KASAHARA and R. YOSHIYAMA, Jahrb. f. Kinderh. **135**:167 (April) 1932.

Kasahara and Fujisawa (*Ztschr. f. d. ges. exper. Med.* **73**:11, 1930) have recorded observations on the spinal fluid of normal animals. The present authors show that in rabbits and dogs, sterile parotitis, caused by injections of Lycopodium, or suppurative parotitis, caused by Staphylococcus aureus, may be followed by the changes in the cerebrospinal fluid characteristic of serous meningitis.

CLAUSEN, Rochester, N. Y.

Nutrition

PUBLIC HEALTH ASPECTS OF FROZEN FOODS. CARL R. FELLERS, Am. J. Pub. Health **22**:601 (June) 1932.

Freezing of food products for transportation or for preservation, when properly done, retains freshness, flavor and character. This is particularly true of sea foods and poultry products. Fruits and vegetables keep well frozen, but bleed freely on thawing. Spoilage occurs quickly on defrosting. Freezing reduces the number of micro-organisms and prevents their multiplication. The presence of vitamins is apparently little affected.

PARKER, Rochester, N. Y.

DRIED LACTIC ACID MILKS AS A LONG CONTINUED DIET FOR INFANTS. JULIUS H. HESS, I. M. CHAMBERLAIN and L. S. ROBINS, J. A. M. A. **98**:1250 (April 9) 1932.

A comparative study of the relative value of dried lactic acid milks, liquid lactic acid milks and sweet milk mixtures as a diet for infants over a long period of time was made on 116 infants. There was no difference in the time of eruption of teeth; the results of monthly estimations of hemoglobin were practically the same; the incidence of infection was the same, and recovery after illness occurred at about the same rate in all groups. The clinical results indicated that dried lactic acid milks can be used under the same conditions as cultured sweet milk preparations or cow's milk acidulated with U. S. P. lactic acid.

BONAR, Salt Lake City.

THE NEED OF LARGER DOSES OF VIOSTEROL IN SEVERE RICKETS (OSTEOMALACIA TYPE). M. JAMPOLIS and SOL LONDE, J. A. M. A. **98**:1637 (May 7) 1932.

While the authors do not advocate the use of large amounts of irradiated ergosterol indiscriminately, since most cases of rickets respond to accepted dosages, from their experience with two cases of severe osteomalacic rickets, large dosage is necessary under such circumstances. An equivalent of 250 cc. of viosterol in oil 250 D was necessary to produce a cure. No toxicity was noted.

BONAR, Salt Lake City.

TREATMENT OF ALIMENTARY TOXICOSIS. S. KARELITZ and BÉLA SCHICK, J. A. M. A. **99**:366 (July 30) 1932.

The authors have evolved a method of treating alimentary toxicosis in infancy based on the plan to permit a longer than usual period of rest for the gastrointestinal tract and to combat dehydration by an intravenous supply of fluid. A twelve hour period of complete oral starvation was given, while intravenous drip with a 5 per cent solution of dextrose was begun, and a transfusion of from 75 to 150 cc. of citrated blood was made. The drip was continued until signs of toxicosis disappeared. Water was given orally at twelve hours, and a diluted milk formula soon after. Among fifty-three patients over a period of two and one-half years there was a mortality of 12 per cent, as compared with an average mortality of 64 per cent. This method of treatment seems to indicate progress in the treatment of this condition.

BONAR, Salt Lake City.

THREE FATAL CASES OF INFANTILE SCURVY, WITH A DISCUSSION OF FEBRILE REACTIONS, POSSIBLY SECONDARY TO ANTISCORBUTIC THERAPY. JOSEPH STOKES, JR., and FRANK C. CAMPBELL, M. Clin. North America **16**:219 (July) 1932.

In certain cases of scurvy, the authors have noted a decided febrile reaction following the administration of orange juice. These reactions have often been

quite marked, but they subsided slowly with the disappearance of the evidences of scurvy. Three cases which terminated fatally are reported. The infants did not appear seriously ill on admission. The temperature in one case was normal, and in the other two 100.4 F. and 101.4 F., respectively. Almost immediately after being given fairly large doses of orange juice, hyperpyrexia and evidences of central nervous system irritation developed, with a fatal termination on the second day in one case and on the third day in two. Autopsy in one case showed congestion and many small hemorrhages into both lower lobes of the lungs, and a small subpericardial hemorrhage. Within the skull, definite subdural hemorrhages were noted, chiefly over the frontal and parietal lobes. A few small extravasations were found between the dura and the skull. On histologic examination, the ganglion cells were found to be swollen and stained irregularly. There were considerable loss of Nissl substance and complete loss of the characteristic patterns. Throughout all sections, there was marked engorgement of the blood vessels, and in one section of the cortex, several extravasations of the blood were noted. While it cannot be stated definitely that the fatal outcome in these cases was precipitated by the administration of antiscorbutic agents, the suddenness with which alarming symptoms developed following such treatment is very suggestive, and demands further investigation.

SMITH, Ogden, Utah.

ACUTE INTESTINAL DISEASES IN INFANTS. W. H. F. WARTHEN, South. M. J. **25**:297 (March) 1932.

The author's study concerns material observed in Baltimore. He finds that a rapid decline in deaths has occurred during the past twelve years in infants under 2 years of age. During this period there have been a marked improvement in the milk supply and a great increase in the health education of the parents concerned.

He believes that external temperature plays a much less important causative rôle than was formerly believed, and that environmental adaptability plays a much greater rôle in diminishing the incidence of these diseases.

The peak of deaths has been showing a tendency to approach the fall season in recent years. Bacillary dysentery seems to be the causative factor of death in more than half of the cases. These figures coincide fairly well with bacteriologic investigations in other studies.

Continued health education with special reference to isolation and proper disposal of stool should be made available if the mortality from these diseases is to be further lowered.

Efforts should be made along the line of obtaining more complete reporting of cases by physicians, with emphasis on the importance of health education in the private practice of medicine.

SCHLUTZ, Chicago.

COPPER AND IRON REQUIREMENTS IN INFANCY. ALLAN PENNY BLOXSOM, South. M. J. **25**:401 (April) 1932.

The author reports a series of fifty-seven cases of infants seen in private practice to whom a solution of copper with iron was given to determine whether there would be any response indicated by the hemoglobin.

The dosage varied from 1 to 1.5 mg. of copper sulphate and from 10 to 15 mg. of iron and ammonium citrate daily. This group of fifty-seven infants showed an average increase of from 5 to 15 per cent in hemoglobin over a group of 104 infants not receiving copper and iron.

The author believes that copper is probably a necessary element in the nutrition of the human body and that it must be supplied to the growing infant in sufficient quantities in conjunction with iron.

The author recommends the use of iron and copper as a routine addition to the diet after birth.

SCHLUTZ, Chicago.

THE CLINICAL DIAGNOSIS OF NUTRITION. L. C. SCHROEDER, Tr. Sixth Ann. Meet. Am. Child Health Comm. **6**:270, 1929.

The author attempts to explain the difficulties in the diagnosis of nutrition. Racial stock, familial idiosyncrasies of growth, previous illness and endocrine dyscrasias are factors increasing the difficulties. Height and weight, he says, are standards of growth and not of nutrition.

His belief is that the amount and quality of muscle and of subcutaneous tissue in relation to the entire skeletal frame is the best index of the nutritional status. Criteria of skeletal builds, girth of muscle and thickness of subcutaneous tissue in all periods from infancy to adult life are needed.

PARKER, Rochester, N. Y.

A CLINICAL STUDY OF POWDERED WHOLE MILK IN INFANT FEEDING. ANDREW E. AMICK, West Virginia M. J. **28**:196 (May) 1932.

A study was made in the coal fields of southern West Virginia of 100 infants fed formulas of powdered whole milk over a period of two years. The powdered milk used was a popular commercial brand. Orange or tomato juice was given early, and cod liver oil was given to all infants. Cereals and vegetables were begun at the age of 6 months. The study included both sick and well babies, aged from 10 days to 3 months, with eleven who were born prematurely.

The average weekly gain of all infants under 6 months was 5¾ ounces (170 cc.) and of those from 6 to 12 months, 4¼ ounces (125.6 cc.). During the two years, there were five deaths from bronchopneumonia, one from septic meningitis and, among those born prematurely, three from acute inanition.

SHAWKEY, Charleston, S. C.

VITAMINS. D. A. WATKINS, West Virginia M. J. **28**:214 (May) 1932.

The author reviews the history of the study of vitamins and discusses their classification, functions and source of supply and the name "vitamins."

SHAWKEY, Charleston, S. C.

THE APPLE TREATMENT IN INFANTILE DIARRHEA. H. ELIAS and M. SCHACHTER, Progrès méd., Aug. 13, 1932, p. 1409.

The authors have used the apple treatment in infantile diarrhea with considerable success, results being definitely obtained in not more than three days. There are three theories as to the efficacy of apples in this condition: (1) that they supply a vitamin deficiency (Popoviciu); (2) that the tannic acid contained in the apple exerts antibactericidal action (Heisler), and (3) that the action is purely mechanical; the mass of apples fill up the intestinal lumen completely, and thus exert a soothing effect on the neuromotor mechanism (Moro). The authors believe that the last theory is the correct one, although the others may be factors. Their method of treatment is to give from 1,500 to 2,000 Gm. of apple a day in five or six meals.

SANFORD, Chicago.

ACTION OF HUMAN MILK IN EXPERIMENTAL RICKETS. FERNANDA BORSARELLI, Riv. di clin. pediat. **30**:191 (Feb.) 1932.

Human milk was fed to rats to learn whether it would prevent or cure rickets. The administration of milk lessened the action of a rachitic diet in producing lesions of the bones. It had a moderately curative action on rachitic lesions. The curative and prophylactic action of human milk was in direct proportion to the amount of milk taken.

The ingestion of irradiated human milk proved toxic to the animals in the quantities given, but it did result in a deposition of calcium.

HIGGINS, Boston.

FORMULA FOR THE DETERMINATION OF THE FOOD RATION IN CHILDREN'S INSTITUTIONS. I. CASTELLI and G. CASTELLANO, Riv. di clin. pediat. **30**: 235 (Feb.) 1932.

Six children were allowed as much food as they cared to take; the number of calories eaten was calculated.

Calories Ingested by Six Normal Children

			Calories Ingested			
Number	Sex	Age, Years	Total	Per Kg. of Body Weight	Per Sq. Cm. of Body Surface	Calories per Unit Weight-Turgor
1	Male	4	2,059	125	32	5.3
2	Female	7	2,260	105	29	4.85
3	Male	11	3,635	123	34	5.02
4	Male	4	1,710	116	28	4.79
5	Female	7	2,559	131	33	5.3
6	Female	4	1,579	145	32	5.7

The unit of weight-turgor is calculated from the formula: $\frac{\sqrt{wt \times ht}}{10}$. The authors believe that this formula is the most practical basis for measuring the normal appetites of children.

The surface of the body affords a satisfactory basis, but is too difficult for use in practical dietetics.

The maximal diet suggested on the Pirquet system approaches closely the figures obtained with these children.

HIGGINS, Boston.

THE BLOOD LIPASE IN EARLY CHILDHOOD. A. TANCA, Riv. di clin. pediat. **30**:321 (March) 1932.

No striking difference was noticed between the lipase contents of the blood of breast-fed and of bottle-fed babies.

In patients with malnutrition of any cause, the blood lipase was lower than normal. In tuberculous patients without malnutrition, the blood lipase was normal.

Irradiation of the infants with ultraviolet rays resulted in increased blood lipase.

Ingestion of butter increased, while ingestion of olive oil decreased, the blood lipase.

HIGGINS, Boston.

THE MAGNESIUM OF THE BLOOD IN CHILDREN UNDER NORMAL AND PATHOLOGIC CONDITIONS. A. CABITTO, Riv. di clin. pediat. **30**:384 (March) 1932.

The author determined the calcium and magnesium contents of the blood in tweny-two normal persons, from 2 months to 34 years of age. He also determined the calcium and magnesium contents in the blood of six children with tracheobronchial adenopathy, in ten cases of rickets and in six cases of rickets complicated by tetany.

From these determinations, he calculated the calcium magnesium ratio for each child. The magnesium content is relatively high during the first year of life and during puberty. It is lowest in adults. The calcium magnesium ratio varies inversely as the magnesium in the blood.

In tracheobronchial adenopathy there is no appreciable variation of the magnesium content of the blood or of the calcium magnesium ratio from normal. In rickets, not complicated by tetany, there is an increase in the magnesium content of the blood and a lowering in the calcium magnesium ratio. When the rickets is accompanied by tetany, there is usually a diminution of the magnesium of the blood, so that the calcium magnesium ratio is normal.

The author notes that the magnesium content is highest in the blood in those years of life when the greatest increase in weight occurs.

HIGGINS, Boston.

INTOLERANCE TO EGG IN MOTHER'S MILK. MARTINEZ VARGUS, Med. de los niños **33**:57 (March) 1932.

Many mothers eat three or four eggs daily, enough to produce symptoms of intolerance in the nursing baby. Occasionally severe symptoms develop, such as vomiting, diarrhea, alimentary intoxication, urticaria, edema of the lips and eyelids and violent abdominal pain. Desensitization should be attempted by subcutaneous injection of milk or peptone an hour before the feeding.

DWYER, Kansas City, Mo.

STUDY OF TRENDS IN APPETITE AND ANTIPATHY TOWARD FOOD IN SCHOOL CHILDREN. HANS FRIESENHAHN, Ztschr. f. Kinderforsch. **40**:1 (April 22) 1932.

An attempt was made to study the traditional and racial antipathies to certain foods in school children. The author shows that this antipathy develops in the later years of school life. This supports the fact that these antipathies are largely the result of an influence from the child's surroundings. The causes of the traditional antipathy are often obscure and may reach back into the early history of a people. Children, of course, have no rational reasons for their antipathy.

REICHLE, Cleveland.

IRON CONTENT IN MILK. A. WALLGREN, Acta pædiat. **12**:153, 1932.

Using a new method for analysis of iron content of biologic material (*Rev. franç. de pédiat.* **7**:596, 1931), the author obtained the following values:

	Minimum Mg. per Liter	Maximum Mg. per Liter	Average Mg. per Liter
Breast milk	0.205	1.056	0.437
Cow's milk	0.140	0.320	0.239
Goat's milk	0.163	0.490	0.356

The age of the mother and the season of the year play no part in determining the iron content of breast milk. Considerable variation was found in the iron figure for the same person at different analyses. In general, the concentration of iron diminishes slightly in the later months of lactation. There is no demonstrable difference between the iron content of breast milk in the first part and in the last part of a single nursing period. The oral administration of 1 Gm. of reduced iron a day for twelve days failed to raise the iron content of the milk.

The higher figures previously reported by other authors for the iron content of cow's milk are shown to be due in many cases to erosion of the metal container.

MCINTOSH, New York.

THE IRON CONTENT IN SOME ANIMAL AND VEGETABLE FOODS COMMONLY USED IN CHILDREN'S DIET. A. WALLGREN, Acta pædiat. **12**:170, 1932.

A large variety of foods were analyzed for iron content. The following table, giving the results for some of the foods rich in iron, renders scant justice to the scope of the original investigation:

	Mg. per 100 Cc.		Mg. per 100 Cc.
Cocoa (Dutch)	74.35	Wheat bran	9.65
Whey-cheese	23.5	Graham flour	3.9
Parsley	4.85	Wheat	1.45
Egg-yolk	4.44	Wheat flour (white)	0.74
Spinach	3.8	Oatmeal	5.1
Nuts	3.2	Oats	3.4
Beef	1.9	Corn	2.02
Peas	1.49	Ground rice	6.08
Lettuce	0.58	Rice	0.67

The high figures in some of these items reflect the accidental addition of iron in commercial handling.

McINTOSH, New York.

Prenatal Conditions

A QUANTITATIVE STUDY OF PLACENTAL TRANSMISSION AND THE PERMEABILITY OF FETAL MEMBRANES AT VARIOUS STAGES OF PREGNANCY. WILLIAM A. LELL, K. E. LIBER and FRANKLIN F. SNYDER, Am. J. Physiol. **100**:21 (March) 1932.

Over 30 per cent of the phenolsulphonphthalein injected into rabbit fetuses in utero was excreted on the twenty-second day of pregnancy. This amount fell to less than 15 per cent on the twenty-ninth day. The reverse was true when the dye was injected into the gestation sac; about 4 per cent was excreted on the twenty-first day of pregnancy, while about 40 per cent was excreted from the sac on the thirtieth day.

NOURSE, Cleveland.

FETAL BLOOD STUDIES: III. THE CHEMICAL NATURE OF ASPHYXIA NEONATORUM AND ITS BEARING ON CERTAIN PRACTICAL PROBLEMS. N. J. EASTMAN, Bull. Johns Hopkins Hosp. **50**:39 (Jan.) 1932.

The author's earlier papers gave the results of studies on oxygen relationships and the lactic acid content of umbilical cord blood. This paper reports a study of the carbon dioxide content, the carbon dioxide tension and the hydrogen-ion concentration of fetal blood in normal and asphyxiated babies. The results have an important practical application in the treatment of asphyxia neonatorum. While there is considerable evidence that the onset of respiration at birth is conditioned by chemical rather than by physical factors, the exact cause remains obscure.

The author concludes as follows: 1. The carbon dioxide tension of fetal blood is normally higher than that of the vein in the maternal arm, the carbon dioxide diffusion gradient between fetus and mother being about 1.3:1. 2. The elevated tension of the carbon dioxide of the mixed fetal blood supplying the brain of the fetus is difficult to reconcile with the apneic state of the fetus in utero, and at present necessitates the assumption that the sensitivity of the fetal respiratory center, in respect to carbon dioxide at least, is definitely depressed. 3. The primary chemical change in the blood in asphyxia neonatorum is a reduction in the oxygen content of the fetal blood to extremely low levels, the blood of the umbilical vein

falling in fatal cases below 1 per cent by volume. 4. The carbon dioxide content of the blood in severe asphyxia neonatorum is slightly lowered as a result of the displacement of this gas from base by the large amounts of lactic acid present. 5. The serum p_H of asphyxiated infants is reduced to the lower limits compatible with life, and in fatal cases may even fall below 7. 6. The evidence indicates that the use of carbon dioxide as a resuscitating agent in asphyxia neonatorum is not only superfluous but may even be harmful, in that it tends to aggravate an already existing acidosis. It is further suggested that other attempts at stimulation, such as slapping and tubbing, may also be deleterious. 7. The conclusion is reached that the chief therapeutic indication in asphyxia neonatorum is for oxygen (or air); the particular method by which the oxygen is administered seems of minor importance, as long as the air passages are clear and the pulmonary alveoli are supplied with adequate amounts of it.

LYTTLE, New York.

CONGENITAL CYSTIC DISEASE OF THE LUNGS. RICHARD L. NELSON, J. Pediat. **1**:233 (Aug.) 1932.

A case of congenital cystic disease of the lung in a 5½ month old infant is reported. There was diffuse, cystic honeycombing of the upper lobe of the left lung with emphysema, yielding physical signs suggesting partial bronchial obstruction. The periodic occurrence of the symptoms is explained by partial bronchial obstruction with relief due to pneumothorax caused by rupture of a cortical cyst.

LEMASTER, Evanston, Ill.

A CASE OF CONGENITAL GOITER. G. CASTORINA, Riv. di clin. pediat. **30**:749 (June) 1932.

The author reports the case of a child born with a large goiter. During the first days of life, there was some difficulty with breathing. The child died at the age of 2 months of malnutrition. At autopsy the thyroid gland weighed 15 gm.; there were scarcity of colloid and considerable connective tissue. The condition was probably not caused by fetal hyperphasia to compensate for hypofunction of the maternal thyroid.

HIGGINS, Boston.

MALFORMATIONS DUE TO COMPRESSION OF THE FETUS. J. SCHOEDEL, Jahrb. f. Kinderh. **136**:215 (Aug.) 1932.

The mother, aged 30, sustained a fracture of the pelvis at the age of 18. At term, an extra-uterine pregnancy was discovered, and a living child was delivered by laparotomy. The numerous malformations found are explained on the basis of the greatly restricted space available for the fetus.

CLAUSEN, Rochester, N. Y.

CONGENITAL DUODENAL STENOSIS. HELENE FORSCHNER-BOKE, Monatschr. f. Kinderh. **54**:414, 1932.

The author gives a clinical report of three cases including four roentgenograms of congenital duodenal stenosis. The abnormality may occur in three types. The obstruction may be due purely to folds of mucous membrane. Again, there may be a narrowing of a portion of the intestine. Finally, there may be a complete interruption of continuity, with the intestine ending blindly.

The symptoms, of course, depend on the type of the obstruction, the strength of the gastric musculature and the nature of the food.

The treatment is surgical, though one patient in whom the diagnosis was partial stenosis was cured by repeated gastric lavage.

GERSTLEY, Chicago.

THE TRANSMISSION OF VASCULAR CHANGES PRODUCED BY VIOSTEROL FROM THE MOTHER TO THE OFFSPRING. AGATHE JUNCK, Virchows Arch. f. path. Anat. **283**:265 (Feb. 5) 1932.

The author observed that two rabbits whose mother had received 48 mg. of viosterol one month prior to their birth showed marked calcification of the aorta. Histologically, these changes corresponded to those found in grown animals following poisoning with viosterol. Control animals did not manifest similar histologic signs. This observation was in agreement with that of Nicole, who found typical calcification in five or six rabbits when the mother had received viosterol during pregnancy. He believed that viosterol was transmitted with the milk to the young rabbits. The present author demonstrated that if rabbits from a healthy mother were nursed by a rabbit that had received viosterol some time before, only slight changes in the aorta were observed, whereas the young of the rabbits given the drug showed marked aortic changes even if nursed by a healthy mother. This would indicate that the transmission of viosterol takes place chiefly in utero.

If the mother was given only small amounts of viosterol (0.5 mg. for eight days), the harmful effect of which was not to be expected until several months later, rabbits born two months later did not show arterial lesions. In a second litter born six months later, vascular changes were present. Their development seemed to depend on the time that the animals were allowed to live. One stillborn rabbit and one that died when 3 days old did not show any changes. A third one was killed on the fifth day; it had macroscopically small yellow patches in the ascending aorta, which microscopically revealed foci of disintegration of the internal media and an affinity of some elastic fibers for hematoxylin. A fourth animal, which was killed at the age of 42 days, showed the same changes, but more markedly. A fifth animal was killed after eight months. It showed the changes seen in mature rabbits poisoned with vigantol. These rabbits did not show signs of disease during life. In rabbits from a different litter the same changes were observed. It was surprising that the young of some rabbits showed changes in the aorta, even if the mother animal had received only a single dose of 2 drops of viosterol. In one instance cited by the author, the viosterol disease was transmitted to a rabbit in the third generation. The mother of this animal had not received the drug.

The author thinks that viosterol produces a metabolic disorder in the rabbit which is transmitted to the young in utero. Transmission of the disease with the milk plays only a minor rôle.

SCHOENTHAL, New York.

CONGENITAL DEVIATIONS OF THE SPINE AS TO BOTH FORM AND SEGMENT. V. ŠVÁB, Časop. lék. česk. **69**:819 (May 30) 1930.

Deviations of the spine are divided into those of morphology and those of deviation in the number of segments, and both are the cause of congenital scoliosis. The five cases presented reveal semivertebrae, synostosis of vertebrae and spina bifida occulta. Putti regards the developmental deviations of form and number as originating in the process of evolution of the embryo and as merely a morphologic symptom of a general developmental defect. All these conditions may be regarded as primarily defects of vertebral aggregation. The causes of defects of the spine do not react locally, but on the whole embryonal structure. It is evident from the cases cited that the defect may be localized, involve a greater section or may involve structures other than the spine. The division of deformities of the spine has been along clinical lines, possibly because so little is known about the teratogenesis of these conditions.

STULIK, Chicago.

FORMS OF HABITUS IN BABIES. W. COHEN, Maandschr. v. kindergeneesk. **1**:182 (Jan.) 1932.

Lederer first concluded that in babies, even in the new-born, types of constitution may be determined. The author criticizes this work and that of others. He made a similar study in a number of babies, and his results are discussed in this article. He concludes that Lederer's somatometric criteria cannot be maintained.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF HYPOPLASIA MANDIBULAE WITH ATRESIA OF THE ESOPHAGUS. J. J. SOER, Maandschr. v. kindergeneesk. **1**:309 (March) 1932.

In a child suffering from hypoplasia mandibulae, atresia of the esophagus also was found. There was no anastomosis with the trachea. The child died when it was 2 days old. Autopsy was not performed.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF CERVICAL RIBS. J. B. STALLING-SCHWAB, Maandschr. v. kindergeneesk. **1**:346 (April) 1932.

In a girl of 4 years with a congenital lesion of the heart (patent interventricular septum) there were also found two cervical ribs, the left one being much larger than the right.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the New-Born

THE ROENTGEN APPEARANCE OF THE CHEST OF THE NEW-BORN INFANT. JOHN T. FARRELL, JR., Am. J. Roentgenol. **24**:140 (Aug.) 1930.

The author presents the results of a series of roentgenograms of the chests of 159 infants made within forty-eight hours after birth and again on the tenth day. Roentgenograms of some of the children were made for the third time at 6 months of age. The still-born infant's chest could not be distinguished from the abdomen, and no differentiation of heart and lungs was present. In the expanded chest after birth and aeration the individual organs, including the great vessels and often the thymus, were differentiated. The spine was quite straight in the lateral view, and the average width of the chest was 9 cm. (9.1 cm. in boys and 8.9 cm. in girls). The average length of the chest was 5 cm. (5.1 cm. in boys and 4.9 cm. in girls). The transverse diameter of the heart was measured on lines drawn at right angles to the midspine. The average was the same in both sexes, i. e., 5 cm., with an extension of 1.8 cm. to the right and of 3.2 cm. to the left. The heart silhouettes were classed as the long narrow, the broad apical with narrow base, the broad apical with broad base and the round globular. In thirty, or one third of the children measured, the thymus was seen. In deep inspiration the thymus may be hidden by the mediastinal structures, while in expiration, owing to the diminution of the space which it occupies and to the fact that it cannot be appreciably compressed, it is forced out over the heart and the lung fields. No appreciable change took place in the contour of the chest or heart in ten days. The striking observation in the roentgenograms of the children at 6 months of age was the similarity in the configuration of the thorax and the thoracic organs to that seen in the same infant at birth.

STULIK, Chicago.

NONRACHITIC CUPPING OF LONG BONES IN THE NEW-BORN. JOHN T. FARRELL, JR., and E. F. BURT, J. A. M. A. **98**:1801 (May 21) 1932.

Forty-eight new-born Negro infants were examined roentgenologically within the first two days of life. In seven cupping of the long bones was found, and at from 5 to 13 weeks of age four of these showed unmistakable evidence of clinical

rickets. Cupping was found roentgenographically in stillborn infants, but histologic preparations revealed no evidence of rickets. The deformity was due to a concave variation at the junction of the zone of proliferating cartilage and the zone of preparatory calcification.

BONAR, Salt Lake City.

SPASMOPHILIC TETANY IN THE NEW-BORN. E. G. MCGAVRAN, J. A. M. A. **99**:115 (July 2) 1932.

In an undersized infant clinically typical spasmophilic convulsions developed thirty-six hours after birth. Determinations of the blood calcium were not made. Under therapy with calcium, viosterol and a sedative, recovery occurred. The author suggests a therapeutic test in cases with symptoms suggestive of spasmophilia.

BONAR, Salt Lake City.

ANEMIA OF THE NEWBORN IN THREE SUCCESSIVE SIBLINGS. LOUIS H. SEGAR and WALTER STOEFFLER, J. Pediat. **1**:485 (Oct.) 1932.

Three cases of anemia in the new-born with recovery are reported. They occurred in successive children of the same parents. The authors believe that the anemia was due to temporarily inadequate erythropoiesis, dependent on some unknown factor.

LEMASTER, Evanston, Ill.

OEDEMA IN THE NEW-BORN. JOHN GIBBENS, Brit. M. J. **1**:837 (May 7) 1932.

In the author's opinion two of the commonest causes of edema in the newly born, either localized or generalized, are cold and sepsis. Cold is a more frequent cause than is sepsis. The author stresses the use of a thermometer which registers subnormal temperature. He also thinks that many children whose death certificates state that they have died of atelectasis, prematurity or congenital debility have really died from the effects of cold. Two cases are reported illustrating the influence of cold. He then discusses the occurrence of edema due to septic influences.

Scleredema and sclerema are discussed briefly as conditions somewhat analogous to edema. A case of edema from sepsis is then reported.

ROYSTER, University, Va.

DEATH FROM RUPTURE OF THE LIVER IN A NEW-BORN INFANT. H. A. PIM and H. CECIL BARLOW, Brit. M. J. **1**:887 (May 14) 1932.

As the title indicates, this is a report of a death from rupture of the liver on the fourth day after birth. A diagnosis of the condition was not made during life, and at autopsy evidence pointed strongly to a rupture of the substance of the liver, a hematoma being held in place, however, by the capsule of the liver. Bleeding must have been gradual and finally copious enough for the liver to burst and its contents to escape into the peritoneal cavity.

ROYSTER, University, Va.

THE IMPORTANCE OF THE PERMEABILITY OF THE CAPILLARIES OF THE SKIN FOR THE OCCURRENCE OF ICTERUS NEONATORUM. F. HOFFMANN and K. J. ANSELMINO, Arch. f. Gynäk. **143**:500, 1931.

In newly born children, the percutaneous cataphoretic application of histamine, which increases the permeability of the vessels of the skin, induces a transient artificial icterus in the wheal before the onset of a general icterus neonatorum. In children who later do not show general icterus, such an artificial icterus can usually be produced. The experiments indicate that for the occurrence and intensity of icterus neonatorum, in addition to an increase in the bilirubin content in the blood, the permeability of the endothelium of the capillaries of the skin plays an important rôle.

KUGELMASS, New York.

ICTERUS NEONATORUM. K. J. ANSELMINO and F. HOFFMANN, München. med. Wchnschr. **79**:1226 (July 29) 1932.

During intra-uterine life the blood of the fetus is not saturated with oxygen. To overcome this deficiency the organism produces an excessive number of erythrocytes. After delivery the new-born infant has an abundant supply of oxygen, and a decrease in erythrocytes follows. The destruction of erythrocytes results in an extrahepatic formation of bilirubin. The bilirubin content of the blood may be high without the occurrence of icterus. This is due to the variation in the permeability of the capillaries of the skin. When, in a new-born infant without jaundice, the permeability of the capillaries of the skin is increased locally by the application of histamine, an area of icterus is produced.

The presence of a high bilirubin content in the blood of the umbilical cord during delivery does not detract from the theory that saturation of the blood with oxygen is the prime factor in the production of icterus. The authors refer to the work of several investigators who found that there was an increase in the oxygen content of the blood of the umbilical cord during labor. Moreover, the normal destruction of erythrocytes and hemoglobin in the latter period of fetal life, during which there is a polycythemia, would tend to increase the bilirubin content of the blood.

In brief, the authors state that icterus neonatorum is due to the destruction of erythrocytes, beginning during labor as a result of improved oxygenation of the fetal blood and continuing after the new-born infant begins to breathe.

BRAHDY, Mount Vernon, N. Y.

FETAL ERYTHROLEUKOBLASTOSIS AND ICTERUS NEONATORUM MALIGNUS. D. Y. KU and Y. LI, Virchows Arch. f. path. Anat. **283**:62, 1932.

The authors describe the case of a fourth child of healthy Chinese parents who died on the fourth day of life with the symptoms of icterus malignus: jaundice, anemia, fever and dyspnea. The three older children of this family suffered from severe neonatal jaundice. The first child is "alive but weak"; the second and third died on the fifth and third day of life, respectively. In this case, an autopsy was performed and foci of myeloblasts, myelocytes and erythroblasts were found in the liver, spleen, wall of the stomach and skin; the atypical cells were also present in the blood vessels. The authors discuss the possible causes of this condition and consider the jaundice as secondary to the erythroblastosis. In cases with similar changes in the blood-forming organs, congenital hydrops has been observed. The case here described is noteworthy because it is the first one observed in a member of the Mongolian race.

SCHOENTHAL, New York.

UROBILIN IN MECONIUM. FRITZ PASSINI, Ztschr. f. Kinderh. **53**:175, 1932.

The sterile meconium of 429 new-born infants was tested for urobilin. Of these, 108, or 25.17 per cent, showed a positive reaction. The possible source of the urobilin in the meconium is discussed.

SHELLING, Baltimore.

Acute Infections

DIPHTHERIA TOXOID PRECIPITATED WITH ALUM. D. M. WALLS, A. H. GRAHAM and L. C. HAYERS, Am. J. Pub. Health **22**:648 (June) 1932.

The method of precipitation used was that described by Glenney and Barn in which the toxoid is completely precipitated by a 2 to 10 per cent solution of alum separated and resuspended in salt solution. The method follows: To 1 liter of toxoid is added 500 cc. of 4 per cent aluminum-potassium sulphate. The flocculent precipitate settles out in four hours. The supernatant fluid is siphoned

off, and the precipitate made up to 1 liter with 0.85 per cent sodium chloride. After storage overnight at 4 C. the supernatant liquid is again siphoned off, and 0.85 per cent sodium chloride solution is added to make 1 liter.

Tests show that 80 per cent of the antigen remains and that 70 per cent of the protein is eliminated. The optimum precipitation time is from two to four hours. This procedure makes it possible to use toxin of any strength and to concentrate the antigen to any desired strength.

A single injection of 1 cc. in ninety-eight children with positive reactions to the Schick test resulted in a negative reaction eight weeks later in ninety-two or 98 per cent.

PARKER, Rochester, N. Y.

AGE FACTOR IN ACTIVE IMMUNIZATION OF INFANTS AGAINST DIPHTHERIA. J. BLUM, J. A. M. A. **98**:1627 (May 7) 1932.

The best response to active immunization with toxin-antitoxin was between the ages of 2 and 4 years. From one fourth to one third of the injections failed to produce immunity in subjects under the age of 9 months, and the least response occurred under 3 months. All infants should be given the Schick test from three to six months after inoculation. Only 2 of 198 persons who died of diphtheria in New York in 1930 had been immunized. There was a 50 per cent reduction in the mortality from diphtheria in 1930 as compared with 1925.

BONAR, Salt Lake City.

THE EFFECT OF TYPHOID FEVER AND OF PREVIOUS TYPHOID VACCINATION ON THE ANTIBODY RESPONSE TO INOCULATION WITH TYPHOID VACCINE. ROY F. FEEMSTER, J. Infect. Dis. **50**:121 (Feb.) 1932.

This excellent article should be read, since it contains many points of practical interest. In short, Feemster showed that the routine injection of three doses of typhoid vaccine may not be as efficient as is believed, and he recommends another dose several weeks or months afterward. He notes that the Widal reaction may not be reliable in a subject who has had a few vaccinations, and that the complement-fixation reaction is no more reliable than agglutination phenomena in the diagnosis of typhoid fever.

TOOMEY, Cleveland.

FLOCCULATION TESTS FOR THE DIFFERENTIAL DIAGNOSIS OF SMALLPOX AND CHICKENPOX. LEON C. HAVENS and CATHERINE R. MAYFIELD, J. Infect. Dis. **50**:242 (March) 1932.

In this paper is described a flocculation test for differentiating between chickenpox and smallpox.

TOOMEY, Cleveland.

THE LEUKOCYTE RESPONSE IN MAN TO DICK TOXIN, WITH SPECIAL REFERENCE TO EOSINOPHIL CHANGES. STUART L. VAUGHAN, J. Infect. Dis. **50**: 315 (April) 1932.

In immunization programs, a slight leukocytosis was observed after the first injection of scarlet fever toxins, the leukocytes being increased while the lymphocytes were not. The basophils and large mononuclear cells were decreased, and the eosinophils increased.

TOOMEY, Cleveland.

BLOOD CULTURE IN RHEUMATIC FEVER. LAURENCE E. COOLEY, J. Infect. Dis. **50**:330 (April) 1932.

The author gives a concise review of the literature and summarizes her own work by calling attention to the fact that the blood cultures of twenty-five children with rheumatic fever remained sterile even after a month's incubation.

TOOMEY, Cleveland.

DISSOCIATION IN STREPTOCOCCUS SCARLATINAE. EDNA DELVES, J. Infect. Dis. **50**:350 (April) 1932.

There is a dissociation of scarlet fever streptococcus into three main types, S, SR and R, i. e., smooth, smooth and granular, and a little irregular and rough.

TOOMEY, Cleveland.

GONORRHEAL DISEASE IN CHILDREN (FEMALE) AND ITS TREATMENT. J. BERNARD BERNSTINE, M. J. & Rec. **135**:289 (March 16) 1932.

The etiology, diagnosis, symptoms, complications, treatment in both the acute and the chronic state and constitutional treatment of gonorrheal disease are discussed in this paper, and then the author draws the following conclusions:

1. Girls of any age, even infants or the new-born, are subject to this disease.
2. Its frequency is very great.
3. The gonococcus is the causative organism.
4. The mode of infection is not always easy to trace. The sexual act is comparatively uncommon in children.
5. Prophylaxis is of prime importance. The use of metaphen ointment has proved encouraging in our hands as a method of treating vulvovaginitis in children.

WILLIAMSON, New Orleans.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **47**:1643 (Aug. 5) 1932.

For the period from June 19 to July 16, 1932, poliomyelitis increased in the Eastern and Pacific regions. Increases were noted also in typhoid fever, particularly in the East, North, Central and South Central groups, and in influenza in all areas except New England. The incidence of diphtheria, scarlet fever and meningitis continued to be low. The mortality from all causes was 10 per thousand. The average mortality for six years during this period was 11.3.

SANFORD, Chicago.

SEPTIC COMPLICATIONS OF DIPHTHERITIC ORIGIN IN CHILDREN. A. BARSKY and E. LANDSMANN, Arch. de méd. d. enf. **35**:463 (Aug.) 1932.

It is common to associate septic processes with angina due to various types of the streptococcus, but the occurrence of remote infections coincident with mild and wholly unsuspected diphtheritic invasions is unusual.

The authors report briefly two such instances, the first showing involvement of the right hip joint and the second an acute nephritis. Specific therapy resulted in prompt recovery.

AMESSE, Denver.

DIPHTHERIA OF THE VULVA. S. VERAS, Arch. de méd. d. enf. **35**:468 (Aug.) 1932.

During the past twenty-five years there have appeared in the literature the reports of twenty-six cases of diphtheria of the vulva in children. It may therefore be considered as comparatively rare. The author adds the report of another case in a girl, 2½ years of age, whose history revealed that six days after an indefinite febrile attack, painful and frequent micturition was noted. Examination of the genitals showed edema of the vestibule and the hymen; there was a thin, viscous superimposed membrane from which a culture was made and the Klebs-Löffler bacillus isolated. Under specific treatment all symptoms promptly subsided. The possibility of children at school becoming infected through toilets contaminated by sputum from diphtheria carriers is stressed by the author.

AMESSE, Denver.

ANTIDIPHTHERITIC PROPHYLAXIS WITH LÖWENSTEIN'S OINTMENT FOLLOWING SUN RAY EXPOSURE AND INUNCTION WITH AN INERT OINTMENT. AUGUSTO FIORENTINI, Pediatria **40**:643 (June 15) 1932.

Prompted by the lack of uniformity of reports as to the immunization value of Löwenstein's ointment against diphtheria, the author selected ninety children between the ages of 2 and 14 years, having positive reactions to the Shick test, and subjected them to the following study:

Twenty children were immunized according to the standard method to serve as controls; each of these children received immunization injections on June 24 and July 8, 1931; two months following the last treatment sixteen, or 80 per cent, gave a negative reaction to the Schick test.

Forty children were immunized by the inunction method of Löwenstein, the content of one tube of the ointment being applied over an area that had been exposed to sunlight to the point of producing erythema (from five to ten minutes) just before the inunction. Each child received such a treatment on June 25 and July 9 and 23, 1931. Of this series, thirty-two, or 80 per cent, gave a negative reaction to the Schick test two months following the last inunction.

Thirty children were given the inunction over an area which twenty-four hours previously had been thoroughly rubbed with an inert pomade (petrolatum and hydrous wool fat) for the purpose of stimulation as a result of friction. Each of these children received one tube of Löwenstein's ointment on Jan. 2, 16 and 30, 1931. Of this series twenty-five, or 83.4 per cent, gave a negative reaction to the Schick test two months following the last inunction.

These results are in accord with those of Faberi, who was unable to obtain a higher percentage of immunization in guinea-pigs by previous exposure to infra-red and ultraviolet rays. They also tend to indicate that an increased percentage of immunization is obtained by previous friction with an inert ointment, which is in accord with the method of Besredka.

SIGNORELLI, New Orleans.

TREATMENT OF PERTUSSIS; EFFICACY OF VACCINE THERAPY. A. PICCIOLI, Riv. di clin. pediat. **30**:397 (March) 1932.

Following a review of the literature regarding various methods of treatment of whooping cough, the author gives the results obtained in fifty children who had been treated by him with antipertussis vaccine. A stock vaccine was used. Between four and twelve injections were given to each patient. Rapid and complete cure was obtained in forty-four cases, and definite improvement in the other six. The pertussis vaccine gives its best action when it is injected during the catarrhal stage.

Twelve other children were treated by the injection of epinephrine hydrochloride. The author concludes that this method is not so satisfactory as vaccine therapy.

HIGGINS, Boston.

MALTA FEVER: TREATMENT WITH VACCINE AND SERUM. ANTONIO SOSTRES GALLIGA, Med. de los niños **33**:68 (March) 1932.

A boy, aged 8 years, entered the hospital acutely ill. He gave a history of anorexia and fever for three months; the temperature was higher during the night. He had pallor, tachycardia, a gallop rhythm, rapid respiration and a greatly enlarged liver and spleen. The Pirquet and Widal tests were negative. The serum agglutinated Brucella melitensis in a 1:1,000 dilution; the blood culture was positive, and the intradermal reaction was weakly positive. An autovaccine was used during the absence of fever, and a serum, the serum of Lorente, during the febrile stage. After more than a year's treatment the child was completely cured. An excellent description of the disease follows this report.

DWYER, Kansas City, Mo.

GONOCOCCAL URETHRITIS IN A BOY OF 6 YEARS. MARTINEZ VARGUS, Med. de los niños **33**:121 (May) 1932.

A boy, aged 6 years, presented the classic symptoms of urethritis, and gonococci were found in the discharge. He was treated with urethral injections of potassium permanganate solutions in a dilution of 1:4,000, followed by the instillation of mild silver protein in a 1:100 solution. Septicemia developed, and the child was given 3 cc. of acriflavine hydrochloride. This resulted in a prompt cessation of fever and urethral discharge.

DWYER, Kansas City, Mo.

A RARE CASE OF INFECTIOUS DISEASES FOLLOWING ONE ANOTHER. ERNO DEUTSCH, Arch. f. Kinderh. **95**:176 (Feb. 5) 1932.

Scarlet fever developed in a child 2½ years old, and the following month he had pharyngeal diphtheria. Several weeks after this, a retropharyngeal abscess was evacuated, which contained hemolytic streptococci but no diphtheria bacilli, although these were still present in the nasal secretions. Two weeks later measles developed, and with this a laryngeal obstruction. Intubation ruptured an abscess, which yielded diphtheria bacilli. Repeated intubation was necessary, and at times resistance was encountered in introducing the tube. It was finally necessary, under bronchoscopy, to scrape the larynx and trachea, freeing them from granulation tissue and dried blood and pus.

The author designates the condition as "tracheobronchitis hemorrhagica sicca."

LESLIE, Evanston, Ill.

THE ORGANIC ACID CONTENT OF THE URINE IN DIPHTHERIA. JOSEPH CSAPÓ, Arch. f. Kinderh. **97**:53 (July 22) 1932.

The organic acid content of the urine was found to be greatly increased during the first three days of diphtheria, but was normal in the later stages. This increase is believed to be caused by the toxin of the diphtheria bacillus. In four cases of follicular tonsillitis, the total urinary organic acid value was normal or only slightly elevated.

LEMASTER, Evanston, Ill.

SURGICAL COMPLICATIONS OF MEASLES. GERTRUD TREPAL, Monatschr. f. Kinderh. **54**:1, 1932.

A review is given of the major surgical complications of measles that occurred in the Finkelstein clinic during the years 1921 to 1930. In 131 of 3,391 cases of measles, major complications developed. The percentage increased somewhat during the last two years, owing mainly to an increase in mastoiditis. This complication is clearly the most important. Of 65 cases, 33 occurred in the last two years. Otitis occurs in two types, the early form developing during or before the stage of eruption and a later form occurring during the desquamative period. The former is considered specifically a measles infection and the latter due to secondary invaders. The former is the less virulent.

Mastoiditis is divided chronologically into three types: One is an early form developing from one to two weeks following the otitis; the second occurs from two to six weeks later, and the third occurs later than six weeks. Thirty-seven of the 65 cases belong to the first type.

All the cases of mastoiditis associated with measles were severe, probably owing to the generally lower resistance of the patients.

The next most important complication was empyema. This likewise has increased during the last two years; 24 such complications are reported for the whole period.

Occasional complications, such as laryngeal stenosis, appendicitis, osteomyelitis and phlegmon are noted. Noma, fortunately, is very rare. All surgical complications of measles are rather severe and require prompt treatment.

The increased complications of the last years are attributed to secondary grippal infections.

GERSTLEY, Chicago.

PLACENTAL MALARIA INFECTION, CONGENITAL MALARIA AND INOCULATION MALARIA. E. THONNARD-NEUMANN, München. med. Wchnschr. **79**:382 (March 4) 1932.

The ease with which the symptoms of malaria have been controlled with quinine or plasmochin, following the treatment of neurosyphilis by the inoculation of malaria plasmodia, has led to the assumption that the malaria in these cases has been cured. As far as the author knows, no one has reported the presence of plasmodia in the spleen, liver or bone marrow in postmortem examinations following treatment by malariotherapy. The author examined pathologic material to determine whether quinine sterilized only the peripheral blood and left the patient with latent malaria. The negative results following provocative reactions do not necessarily rule out latent malaria. Clark found that 7 per cent of the women in the Panama Canal Zone had plasmodia in the placenta, whereas only 3 per cent had parasites in the peripheral blood. Many years later, in the Republic of Panama the author found that the placenta was infected in 20 per cent of the women, among whom only 5 per cent had plasmodia in the peripheral blood. The localization of plasmodia in the placenta explains the occurrence of congenital malaria. Based on his observations the author advises that malariotherapy be limited to those diseases of the central nervous system in which its efficacy has been proved.

BRAHDY, Mount Vernon, N. Y.

POSITIVE SEROREACTION FOR SYPHILIS FOLLOWING INJECTION OF DIPHTHERIA SERUM. C. STERN, München. med. Wchnschr. **79**:583 (April 8) 1932.

During the last three years there have been several reports of positive reactions of the serum for syphilis following the injection of diphtheria serum. The accuracy of the observations cannot be doubted, but the author advises caution in their interpretation. He observed cases with diphtheria-like symptoms, in which the diagnosis was diphtheria but in which the bacteriologic examinations did not confirm the clinical impression. No antitoxin was administered in these cases, but in some of them a transient positive reaction of the serum for syphilis was obtained. Positive reactions for syphilis were also observed following Vincent's angina and infections with spirochetes of balanitis. In other words, positive serologic reactions for syphilis may occur after infections of the throat without the administration of diphtheria serum, but these usually disappear spontaneously. However, they may persist for longer periods if the infectious foci persist.

BRAHDY, Mount Vernon, N. Y.

EXPERIMENTAL STUDIES WITH DIPHTHERIA TOXIN. SLANCK, München. med. Wchnschr. **79**:705 (April 29) 1932.

Slanck believes that death from diphtheria is due to injury to the central nervous system, rather than to cardiac failure. Changes in the cardiac muscles are secondary manifestations. The diphtheria toxin injures the vital centers in the brain, which results in vasomotor disturbances, cardiac manifestations or other clinical symptoms. The author has successfully treated animals following the intravenous injection of toxic doses of diphtheria by the intrathecal administration of antitoxin. He advises the administration of serum by cisternal puncture in toxic cases of diphtheria.

BRAHDY, Mount Vernon, N. Y.

SEROTHERAPY AND ETIOLOGY OF SCARLET FEVER. E. WINKEL, München. med. Wchnschr. **79**:707 (April 29) 1932.

Winkel reports the results of serotherapy in scarlet fever obtained in the Municipal Hospital in Bremen. Serum was administered to patients who were toxic and had an axillary temperature of 38.5 C. (101.3 F.) or higher. If there was no improvement in twenty-four hours, the injection was repeated. The serum

was given intragluteally in doses of from 10 to 25 cc., depending on the age of the patient. The results were encouraging. There was a rapid fall in the temperature and permanent improvement in all symptoms. The incidence of complications was greatly decreased.

BRAHDY, Mount Vernon, N. Y.

SCARLET FEVER ANTITOXIN TITRATION BY THE DICK NEUTRALIZATION METHOD AND BY THE SCHULTZ-CHARLTON SKIN REACTION. J. PROCHÁZKA, Časop. lék. česk. **69**:1341 (Aug. 26) 1930.

Titration of scarlet fever antitoxin is done readily by use of the Schultz-Charlton blanching test, but care must be taken in the selection of cases and in the interpretation of the minimum amount or dilution producing blanching. Older rashes usually give a milder reaction with the same strength of serum. It is always best to use serums of known titer as a check in titrating new serums. It is a good idea to group the serums according to titer for control. The results obtained by the blanching method are essentially the same as those obtained by the Dick neutralization method. Serums of low titer are not made up for therapeutic use. There is some disadvantage in testing the potent serums, because of the larger number of cases needed and the tendency to pseudoreaction. The rapidity of disappearance of the reaction and the number of pseudoreactions point to the disappearance, in the concentrated serum, of the factors that produce the reaction in the native serums. Only mild cases of one day's duration were used, because the subsequent injection of curative serum would interfere with the test. Only the cases in which the intensity of the rash remained at least twenty-four hours could be used for interpretation.

STULIK, Chicago.

POSTVACCINAL ENCEPHALITIS. KAREL URBANEK, Časop. lék. česk. **69**:1462 (Oct. 24); 1498 (Oct. 31) 1930.

The author reviews the history and stresses the study of encephalitis through the analysis of the (1) clinical symptomatology, (2) pathologico-anatomic findings, histology, bacteriology and immunology, (3) etiology, (4) epidemiology, (5) prophylaxis and (6) treatment. Many contemporary authors are cited on these points. Under prophylaxis the summary is: vaccination with a single scarification; primary vaccination between 2 and 6 months, with secondary vaccination at from 5 to 7 years and tertiary vaccination at 14 to 16 years; consideration of the insurmountable resistance of some parents to vaccination; establishment of routine in mass vaccination so that a rigid technic can be carried out by the staff; police pressure not recommended; means to reimburse those who may have had untoward results; intensive cooperation of social, hygienic, school, health and medical agencies. Treatment consists of the injection of the serum of the parents who have had a positive vaccination or of an antivaccine serum developed in the institute from the calves used for making vaccine.

STULIK, Chicago.

BACTERIOLOGIC CONTROL OF DIPHTHERIA CONVALESCENTS AND CARRIERS. APOIS GUTWIRTH, Časop. lék. česk. **69**:1529 (Nov. 7); 1570 (Nov. 14) 1930.

The author cites the index of contagion as follows: diphtheria, 0.1; scarlet fever, 0.4, and measles, 0.95. A review of the literature includes statistics of various authors. It is important to separate the convalescents, depending on the termination of clinical disease, and preferably to treat them out of doors. A rigid technic for the collection and transportation of cultures is elaborated. The various mediums and stains are discussed. The testing of the virulence of diphtheria organisms is important from the standpoint of both the convalescent and the "carrier." Both the intracutaneous and the subcutaneous methods of testing in guinea-pigs are described.

STULIK, Chicago.

SYPHILITIC REACTION IN SERUM OF CHILDREN AFTER INJECTION OF ANTIDIPHTHERITIC SERUM. JAROSLAV PROCHASKA, Časop. lék. česk. **69**:1600 (Nov. 21) 1930.

Review of the literature reveals that the Meinicke microreaction for syphilis may be positive in severe cases of tuberculosis. A positive reaction with some of the tests for syphilis may be obtained in increasing percentage from the third to the tenth day after the injection of antitoxin and again rapidly decreases after that date, so that after several weeks the reactions are essentially negative. In a series of children tested after an injection of diphtheria antitoxin the positive reactions were as follows: Wassermann reaction, 2.8 per cent; Sachs-Georgi reaction, 2.8 per cent; Meinicke clarifying reaction, 10.9 per cent; Kahn test, 12.9 per cent; Meinicke precipitation test, 28.1 per cent; Muller-Ballung reaction, 35 per cent, and Meinicke microreaction, 50 per cent. After an experimental attempt to prove the development of precipitins, hemolytic agents and antibodies, the author's conclusion is that the positive reaction for syphilis is due probably to the presence of heterogenous bodies after the injection of horse serum. As a measure for protection against the wasting of convalescent serum and as a source of absolute diagnosis, a Wassermann test made before the injection of serum, that is, on the patient's first entry into the hospital, is recommended.

STULIK, Chicago.

ERYTHROCYTE SEDIMENTATION RATE IN TYPHOID AND PARATYPHOID B FEVER. H. SÖDERSTRÖM, Acta pædiat. **12**:268, 1932.

In the first week of typhoid the erythrocyte sedimentation rate is approximately normal (from 10 to 12 mm. in one hour, Westergren method); it rises to 14 mm. in the second week, 19 mm. in the third week, 27 mm. in the fourth week and 29 mm. in the fifth week; thereafter it sinks slowly, remaining abnormally elevated for some time after the disappearance of fever.

The erythrocyte sedimentation rate in paratyphoid B fever is elevated early in the disease, averaging 27 mm. in the first week; in the second week it is 29 mm.; in the third, 38, and from then on it falls slowly.

These are all average figures. In paratyphoid fever, complications distort the curve in individual cases; in typhoid fever complications have little effect.

MCINTOSH, New York.

Chronic Infections

TUBERCULOSIS OF THE INTERVERTEBRAL ARTICULATIONS. HOWARD P. DOUB and CARL E. BADGLEY, Am. J. Roentgenol. **25**:229 (March) 1931.

The authors feel that "intervertebral articular tuberculosis" is a better designation than the common term "epiphyseal tuberculosis of the vertebral body," as the disease at times occurs in this region after the epiphysis has united with the body, and as in some cases the lesion occurs away from the epiphysis. It is also a more descriptive term. The discussion of anatomic, pathologic and roentgen changes is followed by a report of three typical cases. The authors' summary follows: Tuberculous infection of the spine usually occurs by the hematogenous route; various types of spinal involvement depend on the blood supply; tuberculous involvement of the intervertebral articulations is emphasized; early diagnosis is difficult because of lack of deformity, and the roentgen examination must be the chief reliance for early diagnosis; early roentgen signs are narrowing of the intervertebral disk, together with erosion of the articular surfaces, but with preservation of body form. Young adults giving symptoms of recurrent attacks of pain in the lower region of the back, sometimes associated with a temporary scoliotic deformity, should be thoroughly examined; this includes taking the history of exposure to tuberculosis or to other infections. The roentgen appearance of the sacro-iliac region in the young may be misinterpreted because of the frequent widening and haziness of the joint that is noted at this period.

STULIK, Chicago.

BISMARSEN IN THE TREATMENT FOR CONGENITAL SYPHILIS. S. O. CHAMBERS and G. F. KOETTER, Arch. Dermat. & Syph. **25**:1065 (June) 1932.

The authors give the results of the treatment of one hundred and eighty patients with hereditary syphilis with bismarsen or bismuth arsphenamine sulphonate. Observation and treatment covered a period of from one and one-half to two and one-half years.

The drug was injected into the gluteal muscles, with special care to vary the sites of injections and to massage areas after treatment. The size of the dose varied with age, and a chart of calculated dosage was followed. Treatments were given twice a week for a course of ten weeks. Rest periods of two weeks or one month separated the courses of active treatment. Most patients received three courses.

Few untoward effects were seen, and the influence on the Wassermann reactions of the blood and, especially, on interstitial keratitis indicated effective results.

The authors believe that if given carefully bismarsen is a safe and effective drug for the treatment of hereditary syphilis.

EKERMEYER, Iowa City.

TUBERCULOSIS AMONG ORIENTAL CHILDREN IN SAN FRANCISCO. LLOYD B. DICKEY, California & West. Med. **37**:105 (Aug.) 1932.

In a study of a group of 250 children of oriental parentage the author reports the following findings: 1. The total incidence of positive tuberculin reactions was 33 per cent, and in the age group from 12 to 14 years, 58 per cent. This is considerably higher than in similar groups taken from the child population at large. 2. The children of the Japanese were infected in larger proportion than were the children of the Chinese in the series. 3. Cases of active tuberculosis and of phlyctenules occurred in a larger percentage of the oriental children than of children of the white race. 4. Children of oriental parentage reacted to intracutaneously administered tuberculin more strongly than did white children.

MARSHALL, San Francisco.

THE TUBERCULIN TEST. ERNST WOLFF and R. S. STONE, California & West. Med. **37**:108 (Aug.) 1932.

From an extensive study of the literature together with clinical studies, the author draws the following conclusions: 1. The intracutaneous test is specific except in children up to 24 months of age, in whom nonspecific reactions are observed in rare cases. 2. The tuberculin test is sometimes negative in apparently healthy children with nodules or calcified tracheobronchial glands shown in the roentgenograms. 3. The exact relation of allergy to immunity in tuberculosis in childhood is unknown. 4. The intensity of the tuberculin reaction increases in proportion to the percentage of children (*a*) having roentgenographic evidence of a pathologic condition in the chest, (*b*) having active tuberculosis and (*c*) having clinical and roentgenographic evidence of tuberculosis. 5. The intracutaneous tuberculin test represents the most satisfactory method for hospitals and dispensaries, and the percutaneous or tuberculin ointment test is the most convenient method for institutions, schools and private practice.

MARSHALL, San Francisco.

EPILEPSY AND CONGENITAL SYPHILIS. KARL A. MENNINGER, J. Nerv. & Ment. Dis. **75**:473 (May) 1932.

Epilepsy is believed to be dependent on a hyperirritable or damaged brain. Syphilis is known to have a predilection for producing irritation and destruction of the brain. Therefore, it is logical to assume that in some instances epilepsy

may be an expression of syphilis of the brain. Many authors are cited to substantiate this condition by actual percentages. The author presents a study of 31 carefully selected cases with indisputable evidence of congenital syphilis and idiopathic epilepsy. He concludes that congenital syphilis can produce convulsions directly and indirectly without the presence of gross lesions of the brain. An excellent bibliography is appended. The author states that from a statistical point of view, when the occurrence of congenital syphilitic epilepsy is compared with the total number of cases of congenital syphilis the former condition must be regarded as unusual. The frequency, however, is not so important as the definite establishment of its occurrence.

JAHR, Omaha.

CONGENITAL SYPHILIS. WINSTON U. RUTLEDGE, South. M. J. **25**:844 (Aug.) 1932.

The author speaks of some of the difficulties met with in the handling of the problem of congenital syphilis. On the basis of a study of fifty-one syphilitic women and sixty-eight congenitally syphilitic children, he discusses many problems related to the diagnosis and treatment of syphilis.

It is difficult to hold to attendance for a satisfactory period of treatment the class of patients represented in a clinic for congenital syphilis.

In many instances the diagnosis of syphilis in pregnant women depends on the evidence obtained by the Wassermann reaction of the blood, and in spite of the possibility of the occasional existence of nonspecific false positive reactions during pregnancy, all women giving a strongly positive Wassermann reaction on one or more occasions may properly be considered syphilitic.

The earlier antisyphilitic treatment in pregnancy is commenced, the better are the mother's chances for bearing a healthy infant, but there is no time limit for beginning treatment, as much good may be accomplished by treatment instituted as late as the eighth or ninth month.

Repeated pregnancies do not constitute an effective cure for syphilis, and much evidence has been accumulated to show that every pregnant woman with a history of syphilis should receive antisyphilitic treatment during that period, irrespective of the duration of her infection, the amount of previous treatment or the period of her seronegativity.

It has also been shown that apparently healthy wives of husbands with treated syphilis should receive antisyphilitic treatment during pregnancy, especially if the husband's infection occurred less than five years before.

The diagnosis of congenital syphilis is dependent on the recognition of symptoms and signs of this disease and on serologic examination of the blood and the spinal fluid, but since it is a recognized fact that the Wassermann reaction of the blood for the first six weeks of infant life is undependable, it should be checked repeatedly during the first six months in questionable cases.

Because of the high percentage of patients with congenital syphilis who may remain symptom-free and seronegative for months or years, the author feels justified in treating all children of syphilitic parents.

The prognosis for a serologic cure of congenital syphilis depends largely on how early treatment is commenced and on how long it is persisted in. The prognosis is good in most cases in which treatment is instituted before the end of the first year, but with the advance of age, the prognosis of untreated cases becomes progressively worse.

SCHLUTZ, Chicago.

POTT'S DISEASE OF THE FOURTH AND FIFTH LUMBAR VERTEBRAE. CECIL P. G. WAKELEY, Proc. Roy. Soc. Med. **25**:786 (April) 1932.

A case of Pott's disease of the fourth and fifth lumbar vertebrae was reported in a boy aged 5 years.

WILLIAMSON, New Orleans.

JUVENILE NEUROSYPHILIS WITH PUPILLARY CHANGES AS THE SOLE CLINICAL MANIFESTATION. C. WORSTER-DROUGHT, Proc. Roy. Soc. Med. **25**:1226 (June) 1932.

A boy, aged 9 years, knocked his head on a lamp post, after which his parents noticed that the pupils of his eyes were unequal. Physical examination showed that the boy was healthy and well nourished. There was a slight depression of the nasal bridge, and the left pupil was dilated and larger than the right and failed to react to light. The Wassermann reaction of the blood was positive as was also that of the cerebrospinal fluid.

WILLIAMSON, New Orleans.

LEUKOPLAKIA AND EPITHELIOMA IN A CONGENITALLY SYPHILITIC PATIENT. MILIAN and PERIN, Bull. Soc. franç. de dermat. et syph. **39**:390 (March) 1932.

This case is similar to one previously recorded except that the patient had congenital syphilis instead of acquired syphilis. A rapidly growing prickle cell epithelioma developed at the site of a leukoplakia of the vulva.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

COMPARATIVE STUDIES OF OLD TUBERCULIN AND ANATUBERCULIN IN THE PIRQUET AND MANTOUX REACTIONS. G. BETTINARDI, Pediatria **40**:653 (June 15) 1932.

A clear description of the principles on which are based the preparation of Petragnani's "diagnostic anatuberculin," in contrast with old tuberculin is given, and the author states his experience in a study of the comparison of these, first in animals and later in a series of patients. His conclusions are summarized as follows:

1. In animals anatuberculin gave more decisive and lasting reactions than old tuberculin.

2. In man the reactions were identical in degree and duration when the method of Pirquet was followed.

3. By intradermal administration anatuberculin in normal concentration reacts more satisfactorily than old tuberculin in dilutions of 1:2,000, 1:1,000 or 1:500.

The author concludes that since anatuberculin requires no dilution and eliminates the danger of contamination from this source, and since it has been demonstrated that anatuberculin produces constant reaction in the presence of specific tuberculous infections only, never gives a reaction in patients free from tuberculous infections and has in no case produced generalized reactions, it must be recognized and used in preference to old tuberculin. He states as an additional advantage of anatuberculin the fact that it retains its diagnostic properties many years after its preparation.

SIGNORELLI, New Orleans.

THE BLOOD LIPASE IN THE BLOOD SERUM OF CHILDREN AFFECTED WITH TUBERCULOSIS. C. ROSSO, Riv. di clin. pediat. **30**:377 (March) 1932.

The author determined the lipase of the blood by the method of Rona and Michaelis, in fifty children with positive tuberculin reactions. He feels that in tuberculosis, especially the pulmonary and meningeal types, there is a greater diminution of the lipase of the blood serum than in other cachectic conditions.

HIGGINS, Boston.

TABES JUVENILIS. W. PIRES, An. da assist. a psicop., 1931, p. 29.

Pires points out that in some interesting cases of tabes juvenilis the symptoms are manifested in children aged between 5 and 6 years. The differential diagnosis between hereditary ataxias (Friedreich's disease and Pierre Marie's heredo-ataxia) and tabes juvenilis is easy if one is dealing with typical forms, but difficult in

the abortive types (*formes frustes*). There are also mixed forms of Friedreich's disease and tabes concomitant in the same person (Raymond). The tendon reflexes are found increased in heredo-ataxia and abolished in Friedreich's disease and in tabes juvenilis. In Marie's heredo-ataxia and in Friedreich's disease signs of the cerebellar series and the bilateral Babinski phenomenon are observed. In tabes infantilis there are no cerebellar symptoms, and the Babinski sign alone is observed in combined tabes. Further factors of the tabetic series are atrophy of the optic nerve, Argyll Robertson pupil and bladder disturbances. Examinations of the blood and the spinal fluid are of unquestionable importance in the diagnosis of tabes. The Wassermann reaction may be positive in the blood. In the cerebrospinal fluid it is almost always positive. Lymphocytosis and hyperalbuminosis may be observed. The Pandy, Nonne-Apelt and Weichbrodt reactions may be positive. The Lange reaction is nearly always positive, and the reaction to colloidal benzoin reveals a precipitation in the syphilitic area. The cases in which the humoral reactions are negative are rare. A systematic examination of the child, from the point of view of the pupillary reactions, eye fundus, tendon reflexes and serologic reactions for syphilitis, will permit, without doubt, an early diagnosis. Specific syphilitic or malarial treatment will give relatively the best results.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

GENERAL TREATMENT OF PULMONARY TUBERCULOSIS IN CHILDREN. LUIS M. PETRILLO, Bol. Inst. internac. am. de protec. a la infancia **6**:63 (July) 1932.

The endeavor has been made to organize the prophylactic activities in Uruguay according to the general characteristics of the climate and the manner in which it might be applied to the treatment of pulmonary tuberculosis in children, some points in the proper diet for the tuberculous child having been fixed.

According to modern ideas, there is no definite difference between highland and lowland and maritime and continental climates; the climate of Uruguay belongs to the lowland group and is either maritime or continental.

The characteristics of a continental climate may be found in the northwestern parts of the republic, the other parts having either a maritime or a coastland climate, according to L. Bernard's classification. The difference between maritime and marine, or oceanic, climates lies in the totally opposite qualities of their atmospherical attributes, the former being characterized by instability and sudden changes in winds, temperature and humidity. The great transparent luminosity of the atmosphere and the intensity of its insolation are other characteristics in which the climate of Uruguay resembles that of the Mediterranean coastlands.

The climate is therefore exhilarating and strongly stimulant, and is indicated in cases of torpid tuberculosis and contraindicated in cases of possible progression with fever. It would be particularly indicated in cases of tuberculosis with surgical complications, but such patients should be kept in wind-protected sanatoriums. For feverish patients, either hemoptysic, progressive or ulcerocaseous, the inland climate is better suited, although its maritime characteristics are not radically changed: The humidity variations are somewhat diminished, but the changes of temperature cannot be avoided, and the natural defenses against the winds, which create in other countries the so-called subclimates or microclimates, hardly exist at all. Uruguay is absolutely at the mercy of the winds.

As to diet, an endeavor has been made to establish a rational program for the feeding of the tuberculous child, carefully distributing and balancing the quality and quantity of the diet. Research has determined that the children of Uruguay eat a ration with a value of over 2,000 calories, which is more than the average ration prescribed in foreign manuals. This might be explained by any of the following statements: that these children eat more, that their metabolism is more active or that the specific caloric value of the foods of Uruguay is inferior to that of the foods of other countries. In view of the difficulties to fix the exact caloric value of the tuberculous child's ration, it will be prudent to allow a free diet, in accordance with the requirements of the child's instinct and needs.

AUTHOR'S SUMMARY.

THE SYNDROME OF DENTAL SYPHILIS. MARTINEZ VARGUS, Med. de los ñinos **33**:154 (June) 1932.

The author describes the defects of the teeth due to syphilis and Hutchinson's triad in the diagnosis of congenital syphilis.

DWYER, Kansas City, Mo.

CLINICAL DIAGNOSIS OF PRIMARY TUBERCULOUS FOCI. BERTHOLD EPSTEIN, Arch. f. Kinderh. **95**:178 (Feb. 5) 1932.

This article is a protest against the attitude that tuberculosis in infancy can be diagnosed only when it has reached the stage of miliary tuberculosis or tuberculous meningitis. The author believes that diagnosis of the primary focus, with determination of location, can be arrived at in a majority of cases by means of careful physical examination. He finds a shortening of the percussion note over the focus and a sense of resistance, ascertained by the finger acting as the pleximeter. There is a similar impairment of resonance in the axilla of the affected side. Little stress is laid on the presence of râles, which are an infrequent occurrence, but a friction rub is considered of great diagnostic significance, as the author believes that pleuritis is always associated with the primary focus in the lung parenchyma. Of twenty-eight cases that came to autopsy, the correct location of the primary focus had been determined clinically in twenty-two.

LESLIE, Evanston, Ill.

TUBERCULOUS INFECTION AMONG THE SCHOOL CHILDREN OF PÉCS. LASZLOV, DOBZAY and PETRANYE, Arch. f. Kinderh. **96**:88 (April 8) 1932.

Pécs, Hungary, is a town of 61,000 inhabitants. Of 5,804 children in various schools who were subjected to the Pirquet test, 1,431 reacted positively. From somewhat higher results obtained with intracutaneous tests, the authors conclude that 42 per cent of the children are infected. More intensive study was made among a smaller group. Of 809 children studied, 238 showed positive tuberculin tests. Of these, 178 were subjected to roentgenologic and clinical study. Seventy-two were normal, 7 showed active tuberculosis, and the others showed increased mediastinal shadows or calcified lymph nodes. Other tables showed the expected influence of crowded dwellings on tubercular infection. Peasants, as a class, were more free from infection than the families working in mines or in more crowded areas.

LESLIE, Evanston, Ill.

CLINICAL DIAGNOSIS OF PRIMARY TUBERCULOUS FOCI AS PRESENTED BY EPSTEIN. KURL DIELL, Arch. f. Kinderh. **96**:180 (May 6) 1932.

Although the points and technic in the physical diagnosis of a primary tuberculous focus are extremely valuable, too little attention is paid to information that can be gained from tests with tuberculin. In early cases, although no reaction may be obtained with a 1:10,000 or a 1:1,000 dilution, a positive reaction is almost invariably obtained with a 1:100 dilution, if an infection is present.

LESLIE, Evanston, Ill.

ADDITION TO THE WORK: "PROGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDHOOD." KURT HASSMANN, Arch. f. Kinderh. **97**:172 (Sept. 9) 1932.

In a previous article the author stated that "the performance of the tuberculin test in infancy was faulty until a short time ago." He had reference to the tuberculin tests made among the infants of Graz in general and not to those performed in the children's clinic, where the technic suggested by Hamburger is used. Since the more frequent use of the tuberculin test, the number of infants with tuberculosis admitted to the children's clinic has considerably increased.

LEMASTER, Evanston, Ill.

LIPASE CONTENT OF THE SERUM OF TUBERCULOUS CHILDREN. A. GRADNAUER, Beitr. z. Klin. d. Tuberk. **77**:725, 1931.

The lipase content was determined by the stalagmometric method of Rona and Michaelis, modified by Willstätter and Memmen. The serum of healthy children and adults shows, on the average, about the same amount of lipase, although large individual variations occur; that of patients with prognostically unfavorable pulmonary tuberculosis shows the level of lipase to be very low. A correlation between the lipase content and the general condition, the extent of the pulmonary involvement and the anatomic character of the pulmonary lesion is not demonstrable. Very low lipase values in pulmonary tuberculosis indicate a hopeless prognosis, but the same is not true in other organic involvement.

PINNER, Tucson, Ariz. [ARCH. PATH.]

THE BIOLOGIC PROPERTIES OF SEVENTY-EIGHT STRAINS OF TUBERCLE BACILLI ISOLATED FROM INFANTS IN LÜBECK. H. J. TIEDEMANN and A. HÜBENER, Beitr. z. Klin. d. Tuberk. **78**:520, 1931.

The strains were obtained both from clinical material and from autopsy material from infants who had been vaccinated in Lübeck, supposedly with B C G. Only two of the strains were not pathogenic for guinea-pigs; these behaved in the same manner as does an undoubted B C G strain. One of these avirulent strains was obtained from autopsy material from a child who had died of a nontuberculous infection; the only tuberculous lesions found were small caseous foci in the mesenteric lymph nodes. The second avirulent strain was obtained from the gastric content of a child who completely recovered from an undiagnosed disease. All other strains were virulent for guinea-pigs, but not for rabbits. Their virulence for guinea-pigs was rather slight, but quite uniform, although they were derived from children with progressive, fatal and healing forms of the disease. Since even the strains from children who had died of acutely progressive tuberculosis showed low virulence for guinea-pigs, it must be concluded that virulence for guinea-pigs is in no way parallel to that for man. The strain "Kiel" which was present in the laboratory in Lübeck at the time of vaccination, and which is an atypical human strain, shows approximately the same degree of virulence for guinea-pigs as do the strains isolated from infants.

PINNER, Tucson, Ariz. [ARCH. PATH.]

THE DANGERS OF CONTACT INFECTION IN CHILDREN THROUGH THE MEDIUM OF TUBERCULOUS NURSES. S. ZEITLIN, Gesundhfürs. f. d. Kindesalt. **6**:401 (Dec.) 1931.

A nurse in a babies' home in Frankfurt died of tuberculosis. The author has investigated the effect on the fifty-eight children in the home, whose ages ranged from 6 months to 4 years. The nurse had come into intimate contact not only with the infants but also with the young children from June, 1928, to September, 1930. The first signs of illness were observed in August, 1930. It was discovered that thirteen of the children reacted positively to a Moro test. (It is to be noted that the author has made the common error of assuming that all the children who responded negatively to the Moro test were not sensitive to tuberculin. Since a Moro test is a mere approximation, as is also the Pirquet test, the author's examination must be regarded as inadequate.) Thirteen of the children were found to react positively to the Moro test; all these children were probably infected by the nurse. In no case was a severe infection discovered. In only one case did the child show a condition which the author calls moderately severe. In five cases nothing was found either clinically or by the use of roentgenograms. (Apparently, however, the examination by roentgen rays consisted only of fluoroscopy, which is notoriously unreliable in cases of pulmonary tuberculosis. Furthermore, the short period of time [eight months] which had elapsed since the beginning of the infection was too short to permit any constructive observations.)

REICHLE, Cleveland.

BASILAR MENINGITIS FOLLOWING TUBERCULOSIS OF THE OPTIC NERVE: REPORT OF A CASE. G. VON SZABO, Klin. Monatsbl. f. Augenh. **87**:805 (Dec.) 1931.

A case of primary tuberculous infection of the optic nerve giving rise to tuberculous basilar meningitis is reported. A girl, aged 6 years, had noticed failing vision in the left eye, without pain or inflammation, for four weeks prior to her admission to the hospital. At the hospital a diagnosis of basilar meningitis of a tuberculous nature was made, and edema of the left disk with retinal hemorrhages and yellowish-gray discolorations of the retina was observed. The patient died eight days later, presenting meningeal symptoms. Histologic examination of the globe showed the retina to be thickened by edema to twice its size; the disk was prominent; edematous, larger hemorrhages were seen in the deeper fibers, and migrating cells were present in the intravaginal spaces. Four millimeters behind the lamina cribrosa the central vessels were surrounded for a distance of 7 mm. by tuberculous granulations, containing epithelioid, round and giant cells. Here the nerve fibers were completely destroyed. The focus in the optic nerve was the primary lesion, as the meningeal symptoms developed over three weeks after the beginning failure of the vision. Similar cases of an ascending meningitis, arising from the eye, are quoted.

STOLL, Cincinnati. [ARCH. OPHTH.]

THE FREQUENCY OF SYPHILIS IN CHILDHOOD. E. ROMINGER and L. SZEGÓ, Monatschr. f. Kinderh. **54**:20, 1932.

This is a statistical survey with reports from many different clinics. The authors complain of the difficulty of gathering exact statistics and also caution one about giving children with congenital syphilis to caretakers without proper precaution. Apparently syphilis in childhood is diminishing in Germany, owing to somewhat improved economic conditions.

GERSTLEY, Chicago.

CHRONIC MILIARY TUBERCULOSIS OF THE LUNGS: A CRITICISM OF THE TERM. WALTER SCHWENK, Monatschr. f. Kinderh. **54**:32, 1932.

Reports of cases accompanied by photomicrographs are given. The author calls attention to a clinical entity, "disseminated pulmonary tuberculosis of childhood." This condition is really tuberculous bronchopneumonia which in many cases runs a chronic course and may be so mild as to be discovered only incidentally during roentgen examination. The roentgenogram, however, reveals exactly the same shadows as in miliary tuberculosis. Hence the disease is often misnamed "chronic miliary tuberculosis." This is entirely a misnomer. Miliary tuberculosis is an acute infection, borne by the blood stream, involving all organs of the body, usually involving the meninges and ending fatally.

The disseminated pulmonary tuberculosis is limited to the lungs and runs a chronic course, in childhood either ending in recovery or terminating in actual miliary tuberculosis. The only similarity between the two conditions lies in the identical roentgen findings.

GERSTLEY, Chicago.

ISOLATION OF TUBERCLE BACILLI FROM THE BLOOD STREAM BY THE LÖWENSTEIN TECHNIC. H. DETTLING, München. med. Wchnschr. **79**:540 (April 1) 1932.

The author spent ten days in the laboratory of Professor Löwenstein in Vienna to study the preparation of mediums and the method of culturing tubercle bacilli. Later he prepared mediums at the Hygienic Institute in Erlangen. On these mediums he obtained a growth when he planted sputum in which tubercle bacilli had been seen microscopically. However, he failed to obtain a single positive culture from specimens of blood from 115 patients with a variety of diseases,

some of which were as follows: tuberculosis of the bones and joints, in 28; active pulmonary tuberculosis, in 22; genito-urinary tuberculosis, in 5; tuberculosis adenitis, in 3; tuberculosis of the skin, in 8, and atypical rheumatic arthritis, in 4.

BRAHDY, Mount Vernon, N. Y.

Internal Diseases

LIPODYSTROPHIA PROGRESSIVA. AARON CAPPER, Arch. Pediat. **49**:155 (March) 1932.

Two cases of lipodystrophia progressiva are reported. One of the cases is unusual because it occurred in a man; most of the reported cases have occurred in females. Both cases showed a marked eosinophilia, an observation hitherto unreported. The cases are discussed with reference to the etiology of the condition, and the conclusion is reached that the disease may result from a condition that might be termed a negative chemotaxis for fat globules, or an interference with the normal deposition and incorporation of the fat globules in the subcutaneous areolar tissues of the face, neck, arms and chest and sometimes of the abdomen.

WADDELL, JR., University, Va.

ROENTGENOGRAPHIC THYMIC INTERPRETATION AS COMPARED TO POSTMORTEM FINDINGS. HILLYER RUDASILL, JR., Arch. Pediat. **49**:178 (March) 1932.

The results in eighty-eight autopsies at the Children's Memorial Hospital in Chicago are reported. There was only one definitely enlarged thymus, a percentage of 1.1 per cent. The writer feels that enlargement of the thymus is probably not as common as uncontrolled roentgen studies would seem to indicate.

WADDELL, JR., University, Va.

RELATION BETWEEN BACTERIA AND TEMPERATURE IN SUBACUTE BACTERIAL ENDOCARDITIS. HARRY WEISS and REUBEN OTTENBERG, J. Infect. Dis. **50**:61 (Jan.) 1932.

One gleans from textbooks that the optimum time for a positive blood culture is at the point of maximum pyrexia. These authors state that if cultures are made just before the expected rise in temperature, more positive results and higher bacterial counts will be obtained. They also conclude that there is no relationship between the severity of the disease and the degree of bacteremia.

TOOMEY, Cleveland.

ACUTE RESPIRATORY INFECTIONS: III. FILTER-PASSING BACTERIA OF THE NOSE AND THROAT IN HEALTH AND IN COLDS. W. C. NOBLE, JR., and D. H. BRAINARD, J. Prev. Med. **6**:1 (Jan.) 1932.

Studies were made of the anaerobic bacteria found in filtered washings from the noses and throats of fourteen persons with colds and eleven normal persons. Most of the bacteria were gram-negative, but a few were gram-positive. One hundred and fourteen strains were studied, seventy-three being grouped tentatively according to their agglutinative reactions.

The gram-positive flora, isolated from one patient with acute catarrhal coryza, consisted of two strains of bacilli, identical culturally and agglutinatively, and one strain of cocci.

The gram-negative flora was much more numerous, the search disclosing minute cocci (not Micrococcus gazogenes) and bacilli of different sizes and forms. The cocci were similar culturally, but of four groups agglutinatively. The bacilli were even more heterogeneous, falling into several cultural and agglutinative

groups; all were distinct from Bacterium pneumosintes, which the authors were unable to find. These groups were distributed with approximately equal frequency among both normal control subjects and persons with colds.

As to the significance of these findings, to quote the authors, the fewness of strains of the gram-positive group and their demonstration in only one subject would weigh against their primary etiologic relationship. The almost universal occurrence of the gram-negative cocci and their innocuousness when injected into rabbits would indicate that they are normal saprophytic flora. The heterogeneity of the gram-negative bacilli, the approximately equal distribution of their groups among normal subjects and persons with colds, and the absence of epidemic strains would make it unreasonable to assign a causative rôle to any one of these organisms, even though it is apparent that pathogens exist among them.

TURNER, Chicago.

COLOSSAL EMPHYSEMA OF THE UPPER EXTREMITIES; FOREIGN BODY IN THE LUNG. E. W. CARPENTER, J. South Carolina M. A. **28**:49 (March) 1932.

A child of 3 years had received 10,000 units of diphtheria antitoxin to relieve dyspnea. Careful taking of the history revealed that a choking spell had occurred while the child was eating peanut brittle. Three days afterward it began to have dyspnea and swelling. The body, neck, entire face and scalp were inflamed. The respiration was not greatly embarrassed. The temperature was 105 F. The chest could not be studied physically because of the crepitation caused by the emphysema. Several fragments of peanuts were removed, and the child made an uneventful recovery.

WESTON, JR., Columbia, S. C.

RENAL INFANTILISM. VLADIMIR MIRULOWSKI, M. J. & Rec. **135**:283 (March 16) 1932.

The condition occurred in a boy 9 years of age. It is reported at length. Other conditions that cause the same general retardation are mentioned and differentiated.

WILLIAMSON, New Orleans.

THE USE OF COPPER AND IRON IN ONE HUNDRED CASES OF SECONDARY ANEMIA IN CHILDREN. GEORGE W. CALDWELL and ROGER H. DANNETT, M. J. & Rec. **135**:286 (March 16) 1932.

The hundred cases of secondary anemia occurred in children aged from 1 month to 12 years. With the administration of copper and iron, the hemoglobin increased from 64 to 84 per cent in four weeks, and the red cells increased from 3,000,000 to 4,000,000. The study showed the value of the treatment of secondary anemia with small doses of iron together with copper in the proper amount to stimulate hematopoiesis. Iron is best utilized in the presence of copper, which is necessary for the synthesis of hemoglobin.

WILLIAMSON, New Orleans.

MANAGEMENT OF THE CHILD WITH A DEFECTIVE HEART. HERMAN M. JAHR, Nebraska M. J. **17**:109 (March) 1932.

The term "defective heart" is used for convenience of terminology rather than for pathologic description. It includes (1) hearts that have been subjected to inflammatory insults resulting in permanent changes, (2) congenitally abnormal hearts with murmurs as the only evidence of the anomalous character and (3) potentially diseased hearts in children subject to rheumatic fever or repeated occurrences of so-called "growing pains," with manifestations of easy fatigue, low resistance and rapid and soft pulse, but with no evidence of heart disease.

The management of the child is stressed, in addition to the attention to be paid to the heart itself. Necessary as well as unnecessary restrictions as to

exercise are emphasized. Parents should be informed as to the seriousness or lack of seriousness in the different conditions. Children are frequently kept out of school because of a cardiac murmur when activities at home are much more strenuous. The child should not be taught to be an invalid unless this is necessitated by the cardiac condition. A general diet is given, and parents are taught to allow the child to live a normal life as far as possible.

HAMILTON, Omaha.

ANAEMIA OF VARIOUS KINDS IN CHILDREN. F. PARKES WEBER and E. SCHWARZ, Brit. J. Child. Dis. **29**:17 (Jan.-March) 1932.

The authors cite an example of each of the following conditions: (1) severe anemia of agranulocytic or aplastic type that turns out to be really of lymphatic leukemic nature; (2) recurrent epistaxis with anemia and temporary slight splenomegaly, without thrombocytopenia; (3) temporary anemia, with lead poisoning as a possible cause; (4) anemia associated with colitic signs and enlargement of the liver, (5) severe secondary or chlorotic anemia in a boy, probably of nutritional or dietetic origin, and (6) Lederer's "acute hemolytic anemia."

LANGMANN, New York.

CHRONIC STREPTOCOCCAL TOXAEMIA. J. D. HINDLEY-SMITH, Brit. J. Child. Dis. **29**:25 (Jan.-March) 1932.

Careful analysis of four hundred cases in which chronic rheumatism occurred led to the suspicion that chronic rheumatism is merely a symptom which appears in various chronic conditions and derangements. On further analysis it was found that by far the greater number of cases fall into one group, and this the author designates as "chronic streptococcal toxaemia" in contradistinction to the group vaguely designated as septicemia and for which the term "acute streptococcal fever" has been suggested.

The author alludes to the comparison between chronic streptococcal toxemia and tuberculous infection, but suggests that a more accurate parallel can be obtained by comparing the effects of chronic streptococcal toxemia with those of syphilis. He indicates a division of chronic streptococcal toxemia into primary, secondary and tertiary stages, but admits that the line of demarcation between the different stages is very indefinite.

LANGMANN, New York.

AN UNUSUAL CASE OF MULTIPLE LIPOMATA IN A BOY AGED TWO YEARS. W. R. BETT, Brit. J. Child. **29**:39 (Jan.-March) 1932.

From birth this boy had been deformed by grotesque swellings projecting from his back like camels' humps. They increased in size very slowly until two months before admission to the hospital at the age of 2 years, when they suddenly started to grow rapidly. Examination of the throat, chest, abdomen and limbs showed nothing abnormal. Two of the tumors were removed, not completely, however, as they extended deep into the muscles of the back and chest. The pathologic examination proved the tumors to be lipomas and not liposarcomas as was at first thought.

LANGMANN, New York.

HEAT IN THE TREATMENT OF CHRONIC RHEUMATISM. A. GORDON WATSON and G. R. P. ALDRED-BROWN, Brit. J. Phys. Med. **6**:201 (Jan.) 1932.

In this article the authors discuss the physiologic basis of heat in the treatment of chronic rheumatism, and attempt to explain the beneficial effects obtained. Three different methods are described: (1) thermal natural mineral water baths, (2) radiant heat followed by massage and (3) general and local diathermy.

HARTMAN, Cleveland.

THE CARDIAC FALLACY IN ACUTE RHEUMATISM. LLEWELLYN JONES LLEWELLYN, Brit. J. Phys. Med. **6**:208 (Jan.) 1932.

The author divides patients with rheumatic cardiac disease into two groups: (1) those who recover without residual cardiac or other condition, that is, the primitive or benign form; (2) those in whom fixed or organic cardiac lesions develop, that is, the aberrant or malignant form. He believes that little can be accomplished in the study of the pathogenesis of acute rheumatic fever by the investigation of organic cardiac disease. He concludes his article with the question, "Would it not be wise to unravel with equal pertinacity the pathogeny of the 'mobile' cardiac arrhythmias, which, when disclosed, would shed light on acute rheumatism itself — illuminating the origin of that 'mobility' which Trousseau held the hall mark of the affection as a whole?" He believes that the underlying morbid process is so-called acute rheumatism and that chorea is one of endocrine autonomic imbalance.

HARTMAN, Cleveland.

PUBERTAS PRAECOX. C. WORSSTER-DRONGHT, Proc. Roy. Soc. Med. **24**:1338 (Aug.) 1931.

A case of pubertas praecox was reported in a girl of 5 years. Menstruation began at 2½ years. The breasts were prominent at birth, but there was a sudden increase in size at the onset of menstruation. Pubic hair appeared at about 4½ years. The child's height was 4 feet 2 inches (127 cm.). A roentgenogram of her skull showed no abnormality. The sella turcica was normal. The patient's intelligence was only slightly below the standard for her age, but there was considerable disorder of conduct. She was careless, committed petty thefts, was inclined to be dirty and used bad language. The report is accompanied by a picture of the patient.

WILLIAMSON, New Orleans.

PRESYSTOLIC MURMUR, POSSIBLY NOT DUE TO MITRAL STENOSIS. D. W. WINNICOTT, Proc. Roy. Soc. Med. **24**:1354 (Aug.) 1931.

The patient, a boy of 11 years, showed a normal heart except that on auscultation a presystolic murmur could be heard, the quality of which was typical of the murmurs due to rather advanced stenosis. The murmur varied with the posture, being absent when the boy stood. There was, moreover, no systolic murmur. The author had come across a few cases of stenosis in definitely rheumatic children with no systolic apical murmur and without detectable carditis in the acute stage. The patient had suffered from measles, chickenpox and scarlet fever, and his tonsils had been removed at 5 years.

WILLIAMSON, New Orleans.

NUTRITIONAL ANEMIA TREATED WITH COPPER. J. GIBBENS, Proc. Roy. Soc. Med. **25**:130 (Dec.) 1931.

This case was reported in a baby, 10 weeks old. After one week's illness with diarrhea and vomiting the child was found to be anemic, the blood count on September 22 being: red blood cells, 3,872,000; white blood cells, 8,000, and hemoglobin, 55 per cent.

The child was given as much sun and fresh air as possible, without much benefit. On September 28 he began to receive a 1 per cent solution of copper sulphate, 20 minims (1.23 cc.) twice a day, and after twenty-three days the blood count read: red blood cells, 4,800,000, and hemoglobin, 73 per cent.

WILLIAMSON, New Orleans.

THE THROMBOCYTOPENIC TYPE OF PRIMARY PURPURA IN AN INFANT OF FIVE WEEKS. R. C. LIGHTWOOD, Proc. Roy. Soc. Med. **25**:138 (Dec.) 1931.

A case was reported in a full-term male infant of healthy parents. He was the second child. The first baby was normal. There were no miscarriages. The Wassermann reaction was negative. The blood picture and course of the illness are given in the report.

WILLIAMSON, New Orleans.

THE EFFECT OF DIGITALIS ON THE T WAVE OF THE ELECTROCARDIOGRAM. E. COELHO, Arch. d. mal. du coeur **24**:746 (Dec.) 1931.

Coelho states that American writers consider inversion of the T wave a sign of sufficient digitalization of the heart. In 1928, the author, working with dogs, came to the conclusion that, "if the T wave was negative before the injection of digitalis (it is frequently found to be negative in the electrocardiogram of the normal dog), digitalis accentuates this negativity. When the T wave was positive, digitalis never caused it to become inverted. We wish, then, to affirm that the inversion of the T wave, when observed in man following large doses of digitalis, should not be taken as a sign of sufficient digitalization, but represents a state of myocardial insufficiency that is shown by the digitalis."

This paper records studies of ten normal dogs and an unstated number of normal human beings, together with twenty-two patients having heart disease. Representative electrocardiographic tracings are reproduced in the text. The conclusions of this work include the following statements: "The presence of a negative T wave after the administration of digitalis — a true electrocardiographic treasure, because of its rarity — has no practical value in indicating the optimum dose of digitalis to employ in the cardiopathic diseases. In this regard the clinical criterion alone should be our guide."

The bibliography refers to the papers of seven writers other than the author.

TURNER, Chicago.

MEAN BLOOD PRESSURE OF THE CHILD IN NORMAL AND CERTAIN PATHOLOGIC STATES. J. BONABA and A. F. SARACHAGA, Arch. de méd. d. enf. **35**:27 (Jan.) 1932.

Although the maximum blood pressure in the child increases in direct proportion to age, the mean, or average, pressure scarcely changes between the ages of 1 and 14. These observers at the University of Montevideo found practically no deviation in 443 children, although the maximum varied from 96 mm. to 137 mm. The writers fix this average at 75 mm. In acute nephritis there is usually a rise in both the maximum and the minimum pressures, often to the extent of 30 or 40 mm.; the mean pressure rises in the same proportion. In typhoid fever and tuberculosis there is a uniform reduction of all three pressures. It would appear from these studies that throughout infancy and childhood the average blood pressure is almost a fixed quantity.

AMESSE, Denver.

GENERALIZED ATHEROMA OF THE PULMONARY ARTERY AND ITS BRANCHES IN A GIRL OF THIRTEEN. E. APERT and P. C. BAILLET, Arch. de méd. d. enf. **35**:147 (March) 1932.

A case of atheroma of the pulmonary artery extending to its smallest subdivisions, in conjunction with a persistent ductus arteriosus, is reported. Ordinarily, the lesion found in instances of arteritis involving the lesser circulation proves to be a mitral stenosis. In this case, while the Wassermann reaction was negative, the habitus of the patient, her retarded development and a series of morphologic anomalies, together with unequal pupils, point strongly to hereditary syphilis.

AMESSE, Denver.

BLOOD PLATELET DETERMINATIONS. E. BENHAMOU and A. NOUCHY, Nourrisson **20**:16 (Jan.) 1932.

Emphasis is laid on the importance of avoiding error by making all counts of blood platelets on the blood of fasting persons. In the new-born examined before they had taken any water or nourishment, the counts varied from 300,000 to 400,000. After feedings were instituted, the counts were slightly higher. The most significant finding was the regular postprandial rise, amounting to as much as 300,000. This rise regularly reached its peak at the end of an hour to an hour and a half and disappeared during the following hour.

McCLELLAND, Cleveland.

ULCER OF THE PYLORUS. Q. BLECHMAN ET AL, Nourrisson **20**:34 (Jan.) 1932.

From the age of 8 months an infant had vomited "coffee ground" material and had had melena. X-ray films showed a defect in the mucosa in the region of the pylorus. This was interpreted as an ulcer. After repeated attacks of melena and vomiting at intervals for several months the child recovered and at the age of 19 months appeared healthy.

McCLELLAND, Cleveland.

ALIMENTARY ANEMIAS OF INFANCY. J. OATHALA, Paris méd. **1**:181 (Feb. 27) 1932.

This condition is seen in the first part of the child's second year, and always appears in children fed exclusively on cows' milk. Infants born prematurely, twins and those congenitally inferior are predisposed. The condition is always associated with rickets or infections. The blood picture is of the chlorotic type; that is, the hemoglobin is reduced proportionately more than the red cells. Treatment consists in foods rich in vitamins, iron and chlorophyl. The source of infection, of course, must be removed.

SANFORD, Chicago.

ETIOLOGY OF BRONCHOPNEUMONIA IN INFANCY AND ITS RELATION TO THE CLINICAL COURSE. A. SIGNA, Pediatria **60**:15 (Jan. 1) 1932.

The author studied the etiology of bronchopneumonia by practicing direct puncture of the infected area *intra vitam* in thirty-five cases. He was able to isolate a single species of bacteria in 70 per cent of the cases. These cases were either primary or secondary to some contagious disease. The micro-organism most frequently encountered was the pneumococcus of Fraenkel; others encountered, in their order of frequency, were: the bacillus of influenza, Diplococcus catarrhalis and the staphylococci.

His conclusions indicate that in secondary bronchopneumonia the causative organism is most frequently that which produces the primary disease (Eberth's bacillus, Löffler's bacillus, etc.), and that the bronchopneumonia produced by Pneumococcus is the most benign, while that due to Pfeiffer's bacillus, whether primary or secondary, always assumes distinct characters of severity.

SIGNORELLI, New Orleans.

PNEUMOCOCCAL PERITONITIS IN CHILDREN. P. DESTEFANIS, Prat. pediat. **10**:99 (March) 1932.

The author reports the cases of two 6 year old girls who were seen in the same month in the Children's Hospital of Alessandria. The first child had been sick for three weeks before admission, and had accommodated herself somewhat to her infection in spite of a continuously down-hill course, with low-grade fever, leukocytosis, anemia, loss of weight and recurring abdominal pain. The history of the onset suggested that she had had a primary pulmonary involvement, although her lungs were clear when she entered the hospital. She had an opera-

tion on the twenty-fifth day of her illness and recovered satisfactorily. The second child came into the hospital in a semimoribund condition on the eighth day of an illness characterized by nausea, vomiting, abdominal pain and progressive prostration. She died two hours after operation. Both children had generalized peritonitis with profuse quantities of pus from which pneumococci were grown.

The author discusses the differential diagnosis and the indications for operation, and lists a good bibliography of the Italian literature on the subject, particularly that of the last decade.

DOOLEY, Kent, Conn.

A CASE OF BILATERAL PULMONARY HYDATID CYSTS. M. SERFATY and O. R. MAROTTOLI, Arch. argent. de pediat. **2**:561 (Oct.) 1931.

The authors report a case of bilateral pulmonary hydatid cysts in an 8 year old girl, complicated on one side by a serofibrinous pleurisy. The symptoms presented were those commonly found in this disease, namely, dry cough, loss of weight, pain in the chest, chiefly on deep inspiration, and later hemoptysis. The presence of serofibrinous pleurisy on one side obscured the typical roentgen picture of the cyst, and not until the fluid was removed was it possible to confirm the diagnosis.

Complete recovery followed the operative removal of the cysts with their basal membranes under local anesthesia.

The authors bring out the importance of roentgen examination in establishing the diagnosis, and they strongly recommend operative treatment in cases of large hydatid pulmonary cysts.

SCHLUTZ, Chicago.

MULTIPLE AORTIC ANEURYSMS IN A CHILD SIX YEARS OLD. M. ACUÑA, P. WINOCUR and G. OROSCO, Arch. argent. de pediat. **2**:576 (Oct.) 1931.

The authors report the case of a 6 year old girl who entered the hospital in a state of a marked cardiac decompensation. The roentgenograms revealed marked cardiac enlargement and a widened mediastinal shadow.

The child died in spite of antisyphilitic and symptomatic treatment. Autopsy revealed five aortic aneurysms along an area 20 cm. long in the thoracic and abdominal aorta. The one just above the semilunar valves was fusiform, while the others were saccular. Histologic study confirmed their syphilitic origin. There were likewise miliary gummas in the myocardium and specific changes in the pulmonary artery and in other organs.

SCHLUTZ, Chicago.

OBSERVATIONS ON JUVENILE DIABETES BASED ON A PERSONAL SERIES OF THIRTY-FOUR CASES OF GLYCOSURIA IN CHILDREN UNDER FIFTEEN YEARS OF AGE. CARRASCO FORMIGUERA, But. Soc. catalana de pediat. **1**:79 (April) 1928.

A discussion of juvenile diabetes from the standpoint of etiology, frequency, symptomatology, diagnosis, prognosis and treatment is given. Four of the author's thirty-four patients with glycosuria were nondiabetic, nine had a family history of diabetes and five died. In treatment the author emphasizes the difficulty of keeping children free from sugar without subjecting them to hypoglycemic shock. He says that children need more protein and are less tolerant of roughage than adults.

WATSON, Elmhurst, Ill.

MEDIASTINAL DIAPHRAGMATIC PLEURITIS. OLIVIO AHUMADA, Rev. chilena de pediat. **2**:562 (Dec.) 1931.

The author reports seventeen cases of this rather unusual condition. It may begin independently, and grave symptoms develop abruptly; it may occur as a complication in the course of an attack of pertussis or of other infectious diseases, for example, measles and diphtheria, or it may complicate pulmonary tuberculosis.

The abrupt and alarming initial symptoms are generally followed by a prolonged subchronic state, which ends finally in resolution or in death.

Prominent pulmonary symptoms are extensive dulness over both bases, with absence of vocal fremitus over the dull areas. Vesicular breath sounds are diminished. There may be pectoriloquy and tubular breathing, especially pronounced during the expirium. Râles are at times heard. In some cases the signs may resemble those of early cavitation.

The roentgenologic examination shows mediastinal shadows in the region of the diaphragm and in the interlobar fissures. There is always fixation of the diaphragm on the affected side. A characteristic triangular shadow is often visualized better if the roentgenogram is taken from an oblique angle.

SCHLUTZ, Chicago.

PYURIA CAUSED BY DYSENTERY BACILLUS. Z. TEVELI, Arch. f. Kinderh. **95**:92 (Dec. 18) 1931.

The author reports three cases of pyelitis in which B. dysenteriae Flexner was the causative organism. He reviews the literature and suggests that if the possibility of the presence of this bacillus were borne in mind, the diagnosis of "pyelocystitis dysenterica" would be made with greater frequency.

LESLIE, Evanston, Ill.

TREATMENT WITH LIVER IN THE ANEMIAS OF INFANCY. FREIDRICH STRUNZ, Arch. f. Kinderh. **95**:98 (Dec.) 1931.

The author reports his experience with a liver extract in the anemias of infancy. In the anemias of premature infants it was not found to be superior to reduced iron, and proved more costly. In four cases of alimentary anemia, however, one of which was associated with scurvy, it brought about rapid improvement. It is probable that the extract supplies some substance of primary importance in the synthesis of hematin, possibly oxyglutamic acid and oxyproline, the acids of the pyrrole ring. The liver extract was used because it was less likely to produce gastro-intestinal disturbances than preparations of fresh liver. The dosage was 0.75 to 1.0 Gm. per kilogram per day, the equivalent of from 50 to 60 Gm. per kilogram of fresh liver. It may be used in combination with other methods of treating anemias, such as injections of iron or of blood. There is a suggestion that the therapy with liver may benefit resistance to intercurrent infections.

LESLIE, Evanston, Ill.

CALCIUM AND POTASSIUM CONTENT OF THE BLOOD SERUM IN RENAL INSUFFICIENCY. H. G. SCHOLTZ, Deutsches Arch. f. klin. Med. **172**:472 (March 21) 1932.

In individual cases of contracted kidney and of acute nephritis, the calcium values of the total serum were low. In the greater number of cases of contracted kidney, the ultrafiltrable calcium was decreased, though the percentage of colloidal calcium was increased. This phenomenon does not depend on the level of the nonprotein nitrogen, but, it is to be assumed, is associated with changes in the protein nitrogen. Elevation of the potassium level of the serum is chiefly to be found in anuria. When the potassium is increased, it occurs in most noteworthy quantities in the colloidal form. The relationship between calcium and potassium in renal insufficiency apparently has no connection with the clinical signs.

DOOLEY, Kent, Conn.

THE X-RAY PICTURE OF THE THYMUS GLAND. P. REYHER, Ergebn. d. inn. Med. u. Kinderh. **39**:578, 1931.

At present, every possible deviation from the supposedly normal mediastinal shadow of the new-born and the young infant is looked on as an enlarged thymus.

Now it is a fact that the roentgen observations during life do not always correspond to the findings at autopsy. Thus cases that roentgenologically show hyperplasia of the thymus, at autopsy disclosed a normal thymus, and vice versa. The author reports the average weight of the thymus of the new-born infant, based on 68 cases, as 11.8 Gm. Roentgenologically he prefers lateral to anteroposterior views, based on an experience of over 200 cases, 68 of which were checked post mortem. However, he advocates taking both anteroposterior and lateral views. He shows a series of pictures in which those affording an anteroposterior view might justify a diagnosis of enlarged thymus, while in those giving the lateral view no enlargement is to be seen; some of these findings were confirmed by postmortem examinations. The author's observations over a number of years, checked in many cases by postmortem examinations, may be summarized as follows: The lateral view is more trustworthy than the anteroposterior view. A thymus weighing only from 1 to 2 Gm. gives a clear retrosternal field, that is, no retrosternal shadow. The larger the thymus, the more marked the retrosternal shadow is, and the entire retrosternal space is obliterated by a thymus weighing 15 Gm. or over. The greater the body weight at birth, the larger the thymus is. Infants who were small at birth, but who gained rapidly, showed post mortem a large thymus. Pasty or fat infants suffering from exudative diathesis practically always showed a large thymus. Atrophic and premature infants had a small thymus, weighing 1 Gm. and under. In most of his patients with stridor inspiratorius congenitus, there was a medium-sized thymus, and in several even a small one, whereas in those with an extremely large thymus, weighing from 45 to 46 Gm., there was no congenital stridor, which, the author remarks, confirms Finkelstein's skepticism concerning the existence of a thymic stridor.

CAPPER, Philadelphia.

CREMASTERIC RESPIRATION IN THE CHILD. H. SECKEL, Jahrb. f. Kinderh. **134**:339 (Feb.) 1932.

In two children, aged about 18 months, suffering from very severe bronchiolitis, the author observed during expiration a rise of the testicle and during inspiration a sinking of the testicle into the scrotum. This reflex seems to occur only in states of marked expiratory dyspnea. He regards it as "atavistic genital protective respiration."

CLAUSEN, Rochester, N. Y.

METABOLIC STUDIES ON CIRCULATORY SHOCK: IV. OXYGEN SATURATION OF THE BLOOD IN PEPTONE SHOCK. E. SCHIFF and A. MAZZEO, Jahrb. f. Kinderh. **134**:362 (Feb.) 1932.

In nine dogs, the authors demonstrated that the venous blood showed a considerable lowering of the oxygen saturation during peptone shock. At this time also, owing to acidosis, the venous blood was able to take up less oxygen from the air.

CLAUSEN, Rochester, N. Y.

PHYSIOLOGY, PATHOLOGY AND METHODS OF EXAMINATION OF THE HEART. L. DOXIADES, Kinderärztl. Praxis **1**:19 (Sept.) 1931.

This is an excellent résumé of conditions of the heart in childhood, but is not adapted to a review.

HUENEKENS, Minneapolis.

DIAGNOSIS AND TREATMENT OF FOREIGN BODIES IN THE LOWER AIR PASSAGES AND IN THE ESOPHAGUS OF CHILDREN. K. AMERSBACH, Med. Klin. **28**:214 (Feb. 12) 1932.

Stenosis of the air passages or of the esophagus, if it appears suddenly, is always suggestive of foreign body. All possible diagnostic methods have to be used in this direction. An obscure form of bronchitis, particularly with foul-

smelling sputum, should always suggest the possibility of foreign body. If all the other diagnostic methods fail, direct endoscopy has to be used. This is particularly true of esophagoscopy. Bronchoscopy is a somewhat more serious procedure. For diagnostic purposes bronchoscopy only of the upper passages is permissible. For removal of foreign bodies, bronchoscopy of the lower passages is often unavoidable, chiefly because the long-continued tracheoscopy usually leads to edema of the glottis which finally makes tracheotomy necessary. All endoscopic instruments have to be in perfect shape, as otherwise in place of one foreign body two may result. The old type of instruments, like the coin forceps, are entirely out of place in this era of esophagoscopy. Rectal anesthesia with avertin is the method of choice for endoscopic procedures.

ZENTAY, St. Louis.

EXPERIENCES WITH THE CHRONIC PYURIAS OF INFANTS AND CHILDREN. W. GRAVINGHOFF and H. VIETHEN, Monatschr. f. Kinderh. **52**:117 (Feb.) 1932.

An interesting clinical study was carried out with nine roentgenograms. The writer discusses the various methods of examination of the urinary passages. The simplest measures, of course, are those of urinalysis and roentgenograms. Should further examination be required, by far the simplest and most efficient of the more technical procedures is that of filling the bladder with a 12.5 per cent potassium iodide solution injected through a thick catheter with a special syringe. Then pressure is gradually increased until the material has ascended the ureters, when the catheter is clamped and a picture taken. The bladder is then emptied and washed out with boric acid solution. If one wishes further information intravenous pyelography is the next measure to be ordered. Finally, one can resort to the cystoscope and ureteral catheterization.

GERSTLEY, Chicago.

Nervous Diseases

CONGENITAL ECTODERMOSES (NEUROCUTANEOUS SYNDROMES) IN EILEPTIC PATIENTS. P. I. YAKOVLEV and R. H. GUTHRIE, Arch. Neurol. & Psychiat. **26**:1145 (Dec.) 1931.

Three types of congenital neurocutaneous syndromes—Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis and angiomatosis of the brain with trigeminal nevi—have been discussed in a series of fourteen case records, illustrating the association of these syndromes with mental defects in epilepsy. All three syndromes exhibited remarkable parallelism in their clinical and pathologic manifestations. All these conditions are the result of congenital maldevelopment appearing electively on organs of ectodermal derivation—the nervous system, eyeball, retina and skin. The article gives an excellent description of the clinical and pathologic characteristics of each condition. Its length, fifty pages, makes an adequate summary impossible, and it should be read in the original.

BEVERLY, Chicago.

THE EFFECT OF HYPERTONIC SOLUTIONS ON CEREBROSPINAL FLUID PRESSURE. GEORGE MILLES and PAUL HURWITZ, Arch. Surg. **24**:591 (April) 1932.

This investigation was undertaken to study the course of the spinal fluid pressure following the intravenous injection of hypertonic solutions. Studies were made on one man and on a series of dogs. The experiments showed that the reduction of cerebrospinal fluid pressure with single doses of hypertonic salt solution and dextrose is transient. A secondary rise occurs which reaches a point much higher than the original level. The author concludes that high concentrations of sodium chloride are definitely toxic, and that recurrent pressure symptoms and the occasional deaths reported are probably due to the secondary rise in spinal fluid pressure.

KAISER, Rochester, N. Y.

BODY WEIGHT IN ONE HUNDRED AND THIRTY-SIX INDIVIDUALS DIAGNOSED AS ESSENTIAL EPILEPTICS. S. M. WEINGROW, J. Nerv. & Ment. Dis. **75**:384 (April) 1932.

This study was suggested by the metabolic phenomena which have lately been associated with the pathology and therapeutics of epilepsy. The weights of one hundred and thirty-six epileptic patients varying from 15 to 60 years in age were analyzed. It was found that the average weight of the group of epileptic patients was less than that of an equal number of normal persons of a similar age and height.

JAHR, Omaha.

CEREBRAL CHANGES IN PNEUMOCOCCUS SEPTICEMIA. H. M. ZIMMERMAN and HERMAN YANNETT, J. Nerv. & Ment. Dis. **75**:386 (April) 1932.

A boy, aged 28 months, had been delivered by cesarean section because of a maternal pelvic anomaly. A profuse nasal discharge, fever, cough and vomiting developed. Two days later he had a generalized convulsion. He was brought to the hospital in deep stupor, with occasional twitching of the right side of the face. Examination revealed spasticity of the right arm and leg and flaccidity of the left extremities. There was a mucopurulent nasal discharge, and the throat was markedly injected. The tendon reflexes were sluggish, and less active on the left than on the right. The Babinski sign was positive on both sides. Physical and roentgen examination revealed consolidation in the right upper lobe. The white blood cells were 22,000; the polymorphonuclears, 75 per cent. The spinal fluid was normal except for increased pressure. Blood cultures were negative at first, but two days after admission they showed pneumococcus type IV. On the day before death there were 500 colonies per cubic centimeters of blood. Sputum cultures injected into a mouse revealed type I pneumococci.

Necropsy showed the following: the mucous membrane of the throat and larynx was markedly congested. The right lung also formed a cast within the pleural cavity; the whole upper lobe was a solid nodular mass. The sinuses and the middle ears were not involved. The brain and spinal cord showed no marked anomalies grossly. Microscopically, however, there was a diffuse infiltration of mononuclear cells in the left meninges (lymphocytic and phagocytic). The cortex was destroyed by degenerative lesions (necrobiosis of ganglion cells).

JAHR, Omaha.

DIATHERMY OF THE BRAIN. J. KOWARSCHIK, Brit. J. Phys. Med. **6**:245 (March) 1932.

The author describes two ways of diathermizing the brain. He claims good results from the use of this method in typical cases of migraine and also in headaches caused by diseases of the frontal sinuses. In addition he notes a decrease in blood pressure in cases of hypertonia, a regaining of consciousness with uremia, an increase in the output of urine in many persons, an increase of the basal metabolism and an effect on the activity of the generative glands.

HARTMAN, Cleveland.

A STUDY OF THE TOTAL EXCHANGE OF WATER SODIUM, POTASSIUM AND NITROGEN IN EPILEPSY. F. B. BYROM, Quart. J. Med. **1**:289 (April) 1932.

The author concludes that a ketogenic diet produces an immediate circumscribed depletion of the extracellular fluid reserves (water and sodium), a less constant and less marked loss of intracellular fluid (water and potassium) and a temporary draft on the mobile protein reserves of the body.

Spontaneous epileptic convulsions were not preceded by any detectable changes in the total exchange of sodium, potassium or nitrogen, in the net water balance or in the several fractions of fluid intake or output that compose the net balance.

The convulsion is attended by a loss of body weight amounting to as much as a kilogram, due to an extrusion of extracellular body fluid.

It is concluded that the epileptic convulsion is not directly conditioned by the degree of hydration of the tissues.

BRADFORD, Rochester, N. Y.

THE FUNCTION AND ACTION OF THE CEREBROSPINAL FLUID. FEDELE NEGRO, Rev. neurol. **2**:790 (Dec.) 1931.

In a case presenting a fistula after removal of a spinal tumor, the patient died twenty days after operation in a state of extreme cachexia. This led the author to perform experiments in which he found that loss of cerebrospinal fluid was followed by apathy, somnolence, hypothermia, muscular asthenia, slowing of the pulse and respiration, falling of the hair and rapid wasting, with death in from ten to fifteen days. Pathologic examination revealed extremely marked atrophy of all the organs.

Animals given injections of cerebrospinal fluid showed more rapid growth, an increase in the amount of hair and earlier maturity. When patients were given from 20 to 30 daily injections of 20 cc., many changes were observed, such as increased blood pressure, basal metabolism, hemoglobin and weight, improvement in physical and intellectual functions, increased sexual activity and some restoration of sexual power. In women, dysfunction of the ovary was corrected, and the nervous disturbances of the menopause improved remarkably. Improvement was specific in cases of diabetes insipidus. This leads the author to state positively that the cerebrospinal fluid has a regulating influence on the metabolism of tissues and is of definite clinical usefulness.

FREEMAN, Washington. D. C. [ARCH. NEUROL. & PSYCHIAT.]

RESEARCHES ON THE PATHOLOGY OF CERTAIN ENCEPHALOMYELITIDES DUE TO VIRUSES. G. MARINESCO and S. DRAGANESCO, Rev. neurol. **1**:1 (Jan.) 1932.

In his report before the International Neurologic Conference at Bern, Marinesco devoted the first part to a study of herpes, rabies, poliomyelitis and zoster, with a few words on typhus. In the second part, he took up in brief the demyelinizing diseases and their pathogenesis.

The findings are based on clinical and pathologic investigation, and particularly on animal experimentation.

1. *Herpes.*—Herpes encephalitis is rare in man, but is easily produced in animals by corneal inoculation. In its centripetal migration the virus produces inflammatory reactions in the nerves, semilunar ganglion and pons, spreading thence into the surrounding nerve tissues and involving the meninges and perivascular spaces and the septums, with marked proliferation of the microglia. Inoculation in other areas produces lesions in ascending fashion; for instance, in cases in which the retina is inoculated the inflammation progresses along the optic nerve. The injection of herpetic virus into the sciatic nerve produces primary lesions in the spinal cord. Section of the nerve prevents the migration of the virus, although it can arrive by the vascular root. It is not yet decided whether the virus travels along the axis cylinders or by the perineural lymphatics, but lymphadenitis is usually present and strong compression of the nerve without section does not prevent the development. The diffusion of the virus in the neuraxis is principally by the perivascular spaces and spinal fluid, less by the intramedullary nerve fibers.

2. *Rabies.*—Lesions in the central nervous system predominate on the side of the bite, especially in the spinal and sympathetic ganglions connected with the bitten area. The nerves often show severe changes, and the spinal ganglions may show necroses that are at times suggestive of zoster. The later progress of the disease takes it principally to the midbrain, where the substantia nigra and the walls of the third ventricle are severely affected. The medulla oblongata is likewise

severely diseased, although less destruction takes place here. Injection of virus into nerves is much more effective if a sensory nerve is used than in a pure motor nerve like the hypoglossal, indicating that the virus travels by the nerve fibers themselves; these fibers can be shown to undergo marked alterations. Immunity to rabies may be transmitted through the placenta, although no lesions are found in the brain. The relation of the Negri bodies to the rabies is of importance. These probably contain the virus, but when the evolution of the disease is rapid these corpuscles are not formed.

3. *Poliomyelitis.*—Poliomyelitic virus follows the root of the axis cylinders rather than the blood stream or fluid, and the primary lesions are often found in the nervous system in the location where these fibers originate or terminate. It is uncertain, however, whether the portal of entry is shown by the development of localized palsies, since the portal is supposed to be the nasopharynx and yet the paralysis often begins in the lowermost segment. The microglial reaction in poliomyelitis is intense and diffuse, rather than perivascular, and the cerebral peduncles develop an appearance like that in epidemic encephalitis. Differences are particularly the absence of inflammatory lesions in the lenticular nucleus in poliomyelitis and the actual destruction of ventral horn cells which does not take place in epidemic encephalitis. Inflammation of the spinal ganglions is not uncommon in poliomyelitis, but the peripheral nerves do not show infiltrating lesions. Hyperplasia of lymphatic structures is common.

4. *Zoster.*—The eruption contains the virus of the disease and does not represent merely a trophic disorder due to inflammation of the ganglion. The large balloon cells are seen to contain intranuclear inclusions; there are inflammatory reactions about the finer branches of the nerve, and the virus follows along the nerve fibers after penetrating into them. These nerve filaments often show destruction of myelin, with release of fat. "The same general factors, such as the least resistance, p_H and oxidation reduction in the tissues (hodogenesis), bring about the transmission and migration of zona virus as herpes virus."

5. *The Demyelinizing Myelitides.*—The division of inflammations of the nervous system into inflammatory lipolytic and lipotrophic does not give a true conception of the difference, because all the demyelinizing diseases are characterized by disintegration of the myelin, which is phagocytized by the microglia. The disintegration is due to digestive hydrolytic ferments, as in other cases of degenerating nerves. Different tissues possess different hydrogen ion concentrations. The skin, for instance, varies from p_H 3.5 superficially to 7.4 or 7.6 in the base. "The increase of hydrogen ion concentration brings about slowing of the phenomena of oxidation and retention in the tissues of products of incomplete oxidation and even acids. Increase in hydroxyl ions has a contrary effect in increasing oxidation. Investigation of the biochemical structure of nerve fibers and nerve centers has shown a diastatic system represented in nerve fibers by iron, primary catalyst in the myelin and lipase which is ordinarily inactive, whereas in the nerve cells the diastatic system is represented by iron and an oxydase attached to the colloidal masses of the cytoplasm. Rabies virus in iso-electric determinations has a p_H between 5.8 and 7.4, possesses a negative charge and tends toward a positive pole. The results of injection of an emulsion containing virus which tends toward the positive pole are different from those of a virus which tends toward the negative pole. This change in the reaction of the medium of herpes virus brings about a change in its virulence. This property is probably possessed by all neurotropic viruses. On the other hand, the oxydases of nerve cells are destroyed when virus attacks gray matter and activates hydrolytic enzymes where the potential is altered."

FREEMAN, Washington. D. C. [ARCH. NEUROL. & PSYCHIAT.]

MENTAL DISEASES OCCURRING IN FAMILY GROUPS. H. GOLDBLADT and A. ZIPES, Arch. f. Psychiat. **93**:423, 1931.

The authors present a study of mental diseases occurring in closely related members of family groups. The studies were undertaken in sixty-seven cases

(thirty-four males and thirty-three females), the patients being members of thirty families. Ten of the patients were studied personally by the authors, whereas the others were studied from the hospital records of patients admitted between 1909 and 1924. The results of the study were: There were four examples of psychosis in mother and daughter, three in mother and son, one in father and daughter, five in brothers, three in sisters, twelve in brother and sister, one in mother, daughter and two sons and one in uncle and nephew.

Of the thirty family groups, twenty-five showed the same type of psychosis in the members of the same famly, the psychoses being: schizophrenia, 17; manic-depressive psychoses, 3; hysterical psychosis, 1; feeblemindedness, 2, and dementia paralytica, 2. The authors found, however, that, although the disease entities were thus shown to be fairly frequently the same in different members of a given family, the actual disease picture differed markedly. This showed itself to such an extent that there was practically no case in which the clinical picture actually coincided in two or more members of the same family. There was a tendency toward anteposition of the psychosis in parents as compared with the children, and in older siblings as compared with younger. A study of other members of these families showed marked hereditary tainting of psychopathic type in all of the families.

The authors believe that the reason for the difference in the clinical pictures of mental diseases in members of the same family are to be looked for in the environmental factors of the different cases.

MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

MICROCEPHALY AND FEEBLEMINDEDNESS. W. KUERBITZ, Arch. f. Psychiat. **94**:172, 1931.

The author presents a study of four cases of feeblemindedness with microcephalic measurements of the skull. The first case was that of a girl, aged 8½ years, with a history of consanguinity in the parents, whose intelligence quotient was 35. The circumference of the head was 44 cm. The second case was that of a boy, aged 7 years, also with a history of consanguinity of the parents, whose intelligence quotient was 31; there were mongolian features and convulsions; the Wassermann reactions were negative, and the circumference of the head was 39.5 cm. In the third case, that of a girl, aged 9 years, with an intelligence quotient of 54, the circumference of the head was 40 cm. In the fourth case, that of a girl, aged 9 years, whose mother was feebleminded, the intelligence quotient was 33, and the circumference of the skull was 46 cm. In all four cases there were definite physical underdevelopment and decreased resistance to disease, and in three the skulls were thickened. All of the patients showed a tendency to increase psychomotor activity and a poor vocabulary. The author undertook a study of the artistic performance of the children, finding that in case 1 there was just a mixture of lines without any form; in case 2, a slight increase in tendency toward form; cases 3 and 4 both showed ability for form, with at times expressions similar to those one finds in mentally diseased persons.

MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

INVESTIGATION OF DELINQUENT, MENTALLY ABNORMAL GIRLS. E. JACOBI, Arch. f. Psychiat. **94**:303, 1931.

The author reports a study of thirty delinquent girls who were referred to the psychiatric clinic because of different forms of mental or emotional deviation. He is particularly concerned with the attempt to ascertain the relative importance of the constitutional and environmental factors in bringing about the states of delinquency, particularly prostitution, and the relationship between these factors and the mental abnormality noted. He comes to the conclusion that, when all things are considered, the constitution of the patient seems to play a much more important rôle than the environmental conditions. He is of the opinion that,

although it is difficult in any given case to decide which one of these two factors contributes more to the final product, it seems definite that the constitutional factor is the more important. This is seen especially in feeblemindedness, and the author agrees with a number of other observers that in these cases, at any rate, the constitutional defect is more instrumental in bringing about the difficulty in adaptation. In such cases the most important symptoms are those of sexual delinquency, shiftlessness, prostitution and venereal diseases. In part of the cases investigated, psychoses such as schizophrenia and dementia paralytica have really led to the delinquency. In other cases, however, the psychoses have developed long after the first signs of delinquency have shown themselves, and have merely increased the difficulty in adaptation. The prognosis in all of these cases is, of course, much poorer than in cases of delinquency in which there is no mental disease, because the combination of the mental disturbances with the poorly constituted character does not seem to lend itself to treatment.

In all of the cases attempts were made to institute psychotherapeutic measures as well as amelioration of the environmental factors, but these were mostly unsuccessful. The study is particularly important because the cases have been observed for a long time, some of them as long as from fifteen to twenty years. The author believes that, although in these cases at least there was an important constitutional factor, the only way of ameliorating the conditions is by changing the environment and placing the patients in situations that will not strain their already weakened ability to adjust.

MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

FINGERTIP CAPILLARIES AND FEEBLEMINDEDNESS. M. SCHMIDTMANN, Arch. f. Psychiat. **94**:470, 1931.

The author reviews and analyzes the reports made in this field by different observers and adds a study of material of his own. The material consists of 280 mentally abnormal persons with conditions that he divides into 7 groups: (1) epilepsy; (2) encephalitis; (3) psychopathy; (4) simple feeblemindedness; (5) feeblemindedness due to gross lesions of the brain; (6) mongoloid feeblemindedness, and (7) cretinism and myxedema. He finds that the most atypical forms of capillaries, that is to say, archetypes and vasoneuroses, occur frequently in all the groups of feeblemindedness, especially in the last one. Intermediary forms are found regularly in all groups, and also in normal persons, and therefore cannot be designated as abnormal. The author stresses that in the literature in general and in the results of investigations of this type the occurrence of differences of opinion is probably due to differences in interpretation of the findings rather than in the findings themselves. Frequently authors designate as one form capillaries that by other authors would be considered as being of some other form. Schmidtmann is of the opinion that atypical capillary forms are phenomena only of general psychophysical inferiority and must be considered as such and not as occurrences in themselves. He thinks that the cause of the occurrence of abnormal capillary forms must be looked for in the condition of the skin and he finds, in cases of feeblemindedness that are associated with diseases of the skin, that the capillaries differ in form in relation to the diseases of the skin.

MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

MENINGITIS. E. GORTER, Maandschr. v. Kindergeneesk. **1**:251 (Feb.) 1932.

The author illustrates with four examples the diagnostic and prognostic difficulties in meningitis. The first two examples are cases of acute meningococcic meningitis or acute aseptic purulent meningitis of unknown etiology; one is a case of meningitis which in the beginning was regarded as tuberculous meningitis and had an unexpectedly favorable course. In the third case, one of chronic meningitis, the etiology remained unknown. In the fourth case also the diagnosis was difficult, and the possibility of Heine-Medin's disease had to be considered particularly.

VAN CREVELD, Amsterdam, Netherlands.

VENTRICULOGRAPHY AND ENCEHALOGRAPHY. H. J. BOEVÉ, Maandschr. v. kindergeneesk. **1**:286 (March) 1932.

The technics of ventriculography and of encephalography as introduced by Dandy are described, and their significance for the recognition of the place of the ventricular block in cases of hydrocephalus and for the localization of cerebral tumors is stressed and illustrated by cases observed by the author.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

SCHOOL MYOPIA. A SORSBY, Brit. J. Ophth. **16**:217 (April) 1932.

This is an excellent review of the modern conception of myopia. The author says that, as much as recent work has clarified the issue, it cannot be said that all established factors are covered by the more modern views. One bed-rock fact, which recent work seems to ignore in its stressing of the essential unity of all spherical errors, is the vastly different behavior of the hypermetropic and myopic eye during school life. It may well be that the progressive hypermetropic and the stationary myopic eyes are but the beginning and the end-stages of the progressive process seen in myopia. It cannot be sufficiently emphasized that myopia develops during school life, particularly after the age when the growth of the eye is regarded as being complete—the age of 8 years.

Most school myopia becomes magnified at about the age of 12 years. If the growth of the eye has ceased by then, why should there be in a certain proportion of children a readjustment of axial length, or the position or strength of the refracting media? This can hardly be a physiologic process if it affects only a small percentage of children.

It is unlikely that the problem of myopia will be solved without intensive study in its breeding ground—the school.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

THE REFRACTION OF CASES OF CONGENITAL TORTICOLLIS ASSOCIATED WITH HEMIATROPHY OF THE FACE. A. SORSBY and M. SHAW, Brit. J. Ophth. **16**:222 (April) 1932.

Nine cases of congenital torticollis associated with definite hemiatrophy of the face were observed. Not only was the affected side of the face grossly smaller than the other, but the diameters of the affected orbit were also smaller. In only one case was there marked difference in the refraction of the two eyes, so that it is justifiable to conclude that influences in the development of the orbit do not affect the state of the refraction of the eye.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

MICROPHAKIA. F. GNAD, Klin. Monatsbl. f. Augenh. **87**:33 (July) 1931.

Both eyes of a girl, aged 5 years, showed congenital relative and absolute smallness of the lens, and megalocornea of 13 mm. in the left eye, and of 13.5 mm. in the right. The central portion of the anterior chamber of the left eye was obliterated by close apposition of the lens and cornea. There was no iridodonesis. The anterior chamber of the right eye was deep; the pupil was crossed by numerous shreds of the pupillary membrane, and the iris and lens showed vivid tremulation. Under homatropine the pupil measured 8 mm., leaving a space of 1 mm. between the margins of the pupil and lens, in which a few frail zonular fibers were noticed. The fundi of both eyes were normal but for a small physiologic excavation in the left disk. Pilocarpine lessened the tension of the right eye, but caused pain, apparently because the iris was pressed against the cornea during the miosis. The tension in both eyes was reduced by extraction of the lenses under special precautions. The lenses were clear, of equal size

and spheroid. The correction in both eyes amounted to 14 convex diopters with 4 diopters cylinder; this would suggest that the globes were abnormally short.

STOLL, Cincinnati. [ARCH. OPHTH.]

CHLOROMA OF THE ORBIT: REPORT OF A CASE. N. BLATT, Klin. Monatsbl. f. Augenh. **87**:209 (Aug.) 1931.

A survey of the ophthalmologic literature, compiled by Blatt, showed the extreme rarity of chloroma of the orbit and the uncertainty of its origin. Some authors consider it a biologic variety of leukemia, others a tumor related to sarcoma. The author's case concerns a girl, aged 3 years, with exophthalmos of the right eye in a completely fixed position. The lids could not be closed, the pupils were large and rigid, the disk was pale and the retinal vessels were normal. Hard and uneven tumor masses could be felt above and below the globe. The left eye was found outside the lids and embedded in brownish-green tumor masses, the size of a hen's egg, which also protruded and showed an uneven surface, partly bleeding and gangrenous. Other tumors could be palpated on the temples and at the border of the scalp on the forehead; smaller nodules were disseminated in the scalp and apparently adherent to the bone. The child was well developed, but either somnolent or excited. Roentgenograms showed an enlarged skull, dilated fissures, periosteal bony formations on the frontal bone and destructions in the sphenoidal, ethmoidal and left zygomatic bones.

The condition of the blood gave no evidence of leukemia. Blatt agrees with Schmaus, who defined chloroma as "round cell sarcoma of the bones, especially of the skull, which contain lipochrome, causing the greenish discoloration." It occurs in persons with an inferior hematopoietic system, based on their embryonic development.

STOLL, Cincinnati. [ARCH. OPHTH.]

CHILDREN AND SPECTACLES. K. T. A. HALBERTSMA, Maandschr. v. kindergeneesk. **1**:209 (Jan.) 1932.

The author discusses the complaints in children that may be caused by disease of the eye and under what circumstances the wearing of spectacles is necessary.

VAN CREVELD, Amsterdam, Holland.

THE LARGE DECREASE OF SCROFULOUS OPHTHALMIA. G. F. ROCHAT, Maandschr. v. kindergeneesk. **1**:298 (March) 1932.

In recent years scrofulous ophthalmia, mostly regarded as a symptom of debility, has occurred less frequently in Holland. This impression was confirmed by the statistics of the author's clinic for diseases of the eye. In 1918, there was a sudden rise in the incidence of this condition, but since then the number of patients has decreased steadily. Other clinics have had the same experience. The question as to how far this ophthalmia has connection with tuberculosis is again extensively discussed.

The decrease in the frequency of the disease is explained by the improvement of the general hygienic conditions, especially among children of the hospital class.

VAN CREVELD, Amsterdam, Holland.

PSEUDOPAPILLITIS. A. HAGEDOORN, Nederl. tijdschr. v. geneesk. **75**:6187 (Dec. 26) 1931.

The author points out the importance of examination of the family and of the use of modern methods of investigation for fixing the differential diagnosis between pseudoneuritis and papillitis. He describes several cases observed by himself (in a family with eleven children three had pseudoneuritis of the optic nerve). He discusses the different forms of pseudoneuritis with prominence of the papilla (by abnormal growth, proliferation of the glia [?]), *Drüsen* in the

papilla, indistinct limitation (glial membrane around the papilla, partial myelinization [?]), pseudo-edema by abnormal growth, proliferation of the glia on the papilla and around the vessel and abnormal forms of the papilla.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Ear, Nose and Throat

OBSERVATIONS FOLLOWING ADENOIDECTOMY. FREDERICK T. HILL, Arch. Otolaryng. **14**:775 (Dec.) 1931.

Although poor results in tonsillectomy are easily recognized, this is not true of poor results in adenoidectomy. The tags left at operation often cause nasal and postnasal discharge, bronchial symptoms, obstruction of postnasal spaces, colds in the head, deafness, otitis media and foci of infection until they are removed. Though there may be regrowth of adenoidal tissue after complete removal, at least 90 per cent (Moore's estimate) of recurrences of adenoidal tissue are the result of tags not removed. The favorite site of these tags is in the roof of the nasopharynx just behind the posterior end of the vomer, though remnants about the eustachian orifices and in the fossae of Rosenmüller are common. Anatomic variations in the configuration of the nasopharynx often cause great difficulty in the removal of all the adenoidal tissue, even in the hands of the best operators. There is too great a tendency on the part of operators, especially the unskilled, to consider adenoidectomy a minor part of tonsillectomy; while adenoidectomy is a simple procedure, it is more difficult to get a clean result in adenoidectomy than in tonsillectomy. Hurry, the handicap of bleeding, dull instruments and the difficulty of working in a blind space are the chief causes of poor results. Visual inspection after operation will show many tags that can be removed; it should be employed as a routine measure.

BARNETT, Chicago.

THE INCIDENCE OF ACUTE OTITIS MEDIA IN INFANTS AND IN YOUNG CHILDREN DURING 1930-1931: VARIATIONS IN THE CLINICAL PICTURE. A. J. CONE, Arch. Otolaryng. **14**:797 (Dec.) 1931.

One hundred and ninety-four of 402 children admitted to the Infants' Ward of the St. Louis Children's Hospital between October, 1930, and April, 1931, were found to have acute otitis media. Associated systemic conditions included pneumonia, septicemia, meningitis, pyuria, nephritis, secondary anemia, anhydremia, athrepsia, diarrhea, injuries at birth, congenital defects and asthma. All cases were carefully studied clinically and from the laboratory point of view, both routine and special examinations being made. The author's summary and conclusions follow:

Summary: "The incidence of acute otitis media and mastoiditis was unusually high during the period of six months between October, 1930, and April, 1931. On the basis of the clinical picture the cases were roughly divided into two groups: those without severe systemic reactions and those with diarrhea, athrepsia and anhydremia."

Conclusions: "In the conclusions taken from the group of cases studied, I wish to give, in part, conclusions previously reported by Dean. 1. 'The symptoms which lead to the discovery of otitis in infants are much more frequently pediatric than otologic.' 2. 'The conditions which decide the choice of treatment in otitis are much more often pediatric than otologic.' 3. 'If otitis is present, it can always be diagnosed.' 4. The varying reactions of an infant to an acute otitis or mastoiditis are not due to any specific type of infection or pathology. The same organisms and similar pathologic changes are seen in all types. 5. The diarrhea and vomiting, with resultant anhydremia and athrepsia, are frequently due to a metabolic change as evidenced by changes in the gastric acidity and the ability of B. coli to remain viable in the stomach and upper intestinal tract. 6. Of the parenteral causes of the metabolic change as evidenced by diarrhea, vomiting, athrepsia and anhydremia, acute otitis with mastoiditis is both frequent and serious."

BARNETT, Chicago.

OSSEOUS ATRESIA OF THE POSTERIOR CHOANAE. W. D. STINSON, Arch. Otolaryng. **15**:101 (Jan.) 1932.

Atresia of the posterior choanae may be membranous or osseous. The former may be due to lack of rupture of the bucconasal membrane in the otherwise normal development of the two cavities, usually in embryos of from the thirty-fifth to the thirty-eighth day, or to a secondary blocking of a previously open choana from epithelial overgrowths. The osseous types may be from bone growing in the already membranous occlusion, or may be anomalies of the internal pterygoid plate of the sphenoid bone.

The condition is usually overlooked though obvious enough when once found. Nasal obstruction with glairy mucus, resulting in dyspnea or cyanosis in the prone position and in nursing, should point toward this condition. It is often mistaken for enlarged thymus. Treatment consists in surgically opening the atresia. Two interesting case histories of osseous atresia are given.

BARNETT, Chicago.

ATELECTASIS FOLLOWING ASPIRATION OF PECANS. J. A. FLYNN, Arch. Otolaryng. **15**:268 (Feb.) 1932.

A case is reported in which a child aspirated pecans; what was thought to be pneumonia developed, with three so-called relapses. Roentgen examination after the third relapse showed atelectasis. A careful history at this time revealed that the pecans had been aspirated, a fact previously missed. Aspirations through the endoscope removed large quantities of pus on four occasions, but the nuts were not seen; they had probably been coughed up soon after their aspiration.

This case illustrates the necessity of a detailed history and roentgen examination in obscure pulmonary conditions.

BARNETT, Chicago.

SPEECH DEFECTS IN CHILDREN. LEOPOLD STEIN and I. J. WOLF, Arch. Pediat. **49**:27 (Jan.) 1932.

1. The following speech and voice disturbances are reviewed: hearing, dumbness, partial and universal stammering, organic peripheral dyslalia, dysarthria, stuttering, rhinolalia, hoarseness and falsetto voice.

2. The problem of speech disturbances is a medical one, as has been stressed by others. A knowledge of medicine is necessary for the diagnosis and treatment of most of these conditions.

3. Stammering and stuttering must be differentiated. The former is a disturbance of the articulation; the latter, a speech hesitating in nature, is dependent on psychic states. Stages of development from early childhood are evident.

4. Organic causes of stammering must always be ruled out because of their importance in prognosis. Common among these are mental backwardness, birth trauma and poor hearing.

WADDELL, University, Va.

ETHMOIDITIS IN CHILDREN. S. P. SCHECHTER, Arch. Pediat. **49**:115 (Feb.) 1932.

Attention is called to the frequency of ethmoiditis in children and to its usual symptoms. The frequency with which sinus diseases are overlooked is deplored. Failure to diagnose these conditions properly is perhaps due to the fact that roentgenology as a means of diagnosis is not so reliable in young children as in adults. Transillumination is frequently unsatisfactory, and subjective symptoms are not well expressed. Frequent colds, with nasal discharge or obstruction, should arouse suspicion of sinus disease. Irritability, anorexia, anemia, headache, irregular temperature, recurring adenitis and chronic bronchitis are signs that one has to consider in diagnosing sinus disease in children. In disease of the joints,

when the tonsils and adenoids are removed and there is no cessation of arthritic symptoms, sinus disease must be seriously considered. Four case reports are given, and the usual methods of treatment discussed. Diseased tonsils and adenoids are believed by the writer to cause 80 per cent of the cases of sinusitis in children.

WADDELL, JR., University, Va.

EPIDEMICS OF SEPTIC SORE THROAT OF MILK ORIGIN; PRESENT STATUS OF BACTERIOLOGY AND EPIDEMIOLOGY. D. J. DAVIS, J. Bact. **23**:87 (Jan.) 1932.

From the author's studies of septic sore throat, the following points, which are quoted in full, seem to be established: "1. The epidemics are sudden, sharp and severe, indicating a massive dosage of the infecting agent.

"2. The sick are largely limited to users of one milk supply. There are relatively few contact infections.

"3. Epidemics rapidly recede when the infected milk supply is cut off or the milk pasteurized.

"4. Usually one cow is found with udder infected with an encapsulated hemolytic streptococcus. This organism produces large mucoid, watery, spreading colonies growing especially well on ascites blood agar. These organisms were observed in the Chicago epidemic of 1910-1911 and have become known since then as the Str. epidemicus.

"5. Experiments indicate that when these streptococci are implanted in the cow's teat, they will rapidly ascend the duct and localize in the udder, causing mastitis. They may continue there for long periods thus giving rise to the carrier state. The udder may or may not reveal gross physical changes.

"6. Similar encapsulated streptococci are uncommon in the throats of normal persons (less than 1 per cent) but more common in infected throats (12 per cent of tonsils). Sporadic cases of septic sore throat indistinguishable from epidemic cases are occasionally seen. From such throats encapsulated streptococci of the epidemicus type may be found.

"7. These encapsulated streptococci produce toxins which give rise in animals to specific neutralizing antiserum. The toxins cause specific skin reactions in susceptible persons (differing from scarlet fever toxin). A study of several strains indicates that they are heterogeneous by the agglutination test. Agglutination tests however are often unreliable for encapsulated organisms. We have not as yet compared the toxin antitoxin properties of a number of different strains.

"8. From a study of many epidemics of septic sore throat, it appears that not infrequently cases of scarlet fever and erysipelas occur as complications. There is marked variation in this respect. At times scarlet fever and skin rashes are relatively common. Again they may be rare or absent and erysipelas relatively common. On the other hand it is well known that sore throat without rash is common during epidemics of scarlet fever.

"9. Strains of streptococci classed as scarlet fever or erysipelas organisms on the basis of skin and other tests at times develop capsules and grow quite like strains of Str. epidemicus. Such strains may be the cause of milk-borne scarlet fever. The variability in these clinical manifestations together with the variability in properties of streptococci from epidemics of septic sore throat, scarlet fever and erysipelas suggest the possibility of a variable toxigenic and serologic property.

"10. A study of the world distribution of epidemics of septic sore throat of milk origin reveals three general localities; namely, (*a*) Great Britain, (*b*) Scandinavia and Denmark and (*c*) United States and Canada. In other parts of the world the methods of treating milk supplies may explain their freedom from infections."

STOESSER, Minneapolis, Minn.

SINUSITIS IN CHILDREN. WARREN B. DAVIS, Pennsylvania M. J. **34**:305 (Feb.) 1931.

The author cites anatomic considerations attendant on the development of the paranasal sinuses in early life and states that from earliest infancy sinusitis is a condition to be considered clinically, occurring in the different sinuses in descending order (ethmoid, maxillary, sphenoid and frontal). Two groups of predisposing etiologic factors are enumerated: (1) local conditions interfering with nasal ventilation and drainage, enlarged infected tonsils and adenoids, swollen mucosa from allergic conditions, anatomic defects and malformations, foreign bodies and tumors, and (2) lowered general resistance from poor hygiene, unbalanced diet, metabolic disturbances and endocrine disorders. The condition occurs also as a sequel to measles, scarlet fever, acute bronchitis, pneumonia, pertussis and diphtheria. Among the diagnostic methods, transillumination is of less value than correctly interpreted roentgenograms. As most cases of acute and subacute sinusitis respond to general and local treatment, beyond the removal of infected tonsils and adenoids, surgical measures should be employed conservatively, should be preceded by careful study of roentgenograms, and should be marked by good judgment, accurate anatomic knowledge and refined surgical technic.

HALL, Uniontown, Pa.

BRONCHOSCOPY IN CHILDREN. ANDRÉ BLOCH and A. SOULAS, Bull. Soc. de pédiat. de Paris **29**:398 (July) 1931.

The authors review the indications for bronchoscopy in children, e. g., foreign bodies in the bronchi, bronchial obstruction due to papillomas, congenital stenosis, inflammatory stenosis and bronchopulmonary suppuration. The narrowness of the epiglottic opening is discussed, and the question of the advisability of performing tracheotomy and then "inferior" bronchoscopy, as opposed to "superior" bronchoscopy, which has in some instances been followed by subglottic edema, is mentioned. The latter condition need hardly occur if an instrument of the proper size for each particular case is used, and the bronchoscopist's technic is good. The conclusion reached is that peroral bronchoscopy without any anesthesia, general or local, in the child, is not a dangerous procedure in proper hands, and should be used whenever it is indicated.

BENJAMIN, Montreal, Canada.

BACTERICIDAL POWER OF BLOOD DURING TONSILLITIS. W. VOGEL, Deutsches Arch. f. klin. Med. **172**:298 (Dec. 21) 1931.

During the course of every case of acute tonsillitis, the bactericidal power of the blood decreases, and it increases slowly with the clinical improvement of the patient. With one exception, none of Vogel's patients had complications.

DOOLEY, Kent, Conn.

INVESTIGATION WITH X-RAYS WHEN THE SYNDROME OF GRADENIGO IS PRESENT. H. BURGER, Nederl. tijdschr. v. geneesk. **75**:6003 (Dec. 12) 1931.

By the syndrome of Gradenigo is meant the paralysis of the abducens nerve occurring mostly in acute and seldom in chronic inflammations of the middle ear, usually in young people on the side of the affected ear, and combined with symptoms of irritation of the trigeminus nerve on the same side. The syndrome is also known as the syndrome of the point of the pyramid of the os petrosum. The course is generally favorable. The author examined two patients and came to the following conclusions. Paralysis of the external rectus nerve occurring during an (acute) inflammation of the middle ear may have several causes: It may be independent of the latter and caused by a simultaneous infection, or it may be a

symptom of an otogenic diffuse meningitis, i. e., increased intracranial pressure. In cases in which there are also symptoms of irritation in the region of the sensory branch of the trigeminus, the paralysis is, however, as a rule caused by an inflammation in the point of the pyramid of the os petrosum, proceeding from the middle ear (syndrome of Gradenigo). Roentgen examination in those cases is of great diagnostic value.

VAN CREVELD, Amsterdam, Holland.

Diseases of the Skin

THE INJECTION TREATMENT OF CAVERNOUS HEMANGIOMAS: REPORT OF A CASE AND HISTORICAL REVIEW. S. E. LIGHT, Arch. Dermat. & Syph. **24**:992 (Dec.) 1931.

The author reports the case of a salesman, aged 20, who had had a cavernous hemangioma on the lower portion of the left leg and ankle since birth. The symptoms and size of the tumor had increased prior to treatment. He received thirty-four injections into the mass, nine of which were of 30 per cent sodium salicylate; the remainder were of 75 per cent invert sugar solution. This treatment was carried on over a period of eight months, and only the superficial nevi remained, with no symptoms.

From a review of the literature it is found that the process of injecting irritating chemicals into blood vessels with the object of producing sclerosis has been practiced since 1851 with varying success. The old treatments were painful, and the mortality from infections was high. The most preferred chemicals at the present time are sodium salicylate, invert sugar or a combination of quinine and ethyl carbamate. These chemicals have been infrequently used in the treatment of angiomas, because physical agents, such as radium, roentgen rays, carbon dioxide snow, high frequency electric currents and surgical procedures, are still preferred by many.

The author feels that chemical agents give the best results in the large and deep cavernous hemangiomas. There are also less scarring, less pain and less disability.

HENNING, Iowa City.

GENERALIZED SCLERODERMA IN CHILDREN: REPORT OF THREE CASES AND REVIEW OF THE LITERATURE. E. LAWRENCE OLIVER, Arch. Dermat. & Syph. **25**:72 (Jan.) 1932.

The author reports three cases of generalized scleroderma in children, all of whom were slightly over 3 years of age. They presented roughness, firmness and thickening of the skin over the entire body. The skin appeared fixed to the underlying tissues. One patient received thyroid extract for a short time; the other two were untreated. Two of the patients completely recovered, and the third was markedly improved. Thyroid extract was not credited with the cure in the patient who received it for so short a time.

The etiology of scleroderma is a much discussed point. Some feel that disturbed function of the internal secreting glands is the underlying factor, while others consider acute infections, disturbances of the sympathetic nervous system or marked climatic changes to be the causative factor. The most logical idea is that, whatever the dominant cause may be, these disturbances seem to act as the precipitating factor. There have been very few cases of generalized scleroderma reported in children. The prognosis for children is much brighter than that for adults. Atrophy takes place most often in cases in which the edematous stage precedes the induration. Thyroid extract should be given a trial in all cases. The skin of patients suffering from generalized scleroderma shows definite pathologic changes in the collagenic and elastic tissue, with secondary cellular changes.

HENNING, Iowa City.

PEMPHIGUS: RECOVERY FOLLOWING LONG-CONTINUED COLONIC IRRIGATIONS AND ARSENIC BY MOUTH. JAY FRANK SCHAMBERG, Arch. Dermat. & Syph. **25**:134 (Jan.) 1932.

The author states that there is much that is unknown about pemphigus regarding both cause and treatment. In the United States it is seen as a disease chiefly affecting the Jews of eastern European birth. They seem peculiarly susceptible to it, and when they contract it there is little hope of recovery.

Complete recovery from pemphigus in a Russian Jew, aged 48, is reported. The patient showed a bullous and pustular eruption. The eruption did not seem to have any special area of predilection, and the lesions did not occur in groups but were discrete. After about three months of various types of treatment which gave no benefit, colonic flushings three times a week and potassium arsenite by mouth three times a day were used. In the course of nine months the patient was well. The colonic irrigations seemed to be the main curative factor.

HENNING, Iowa City.

THERAPEUTIC USES OF BACTERIOPHAGE IN THE PYODERMIAS. ANTHONY C. CIPOLLARA and ADELE E. SHEPLAR, Arch. Dermat. & Syph. **25**:280 (Feb.) 1932.

The author reports a study of 108 unselected cases of pyodermia treated with Gratia polyvalent staphylococcus bacteriophage. Only those cases the cultures of which contained a staphylococcus experimentally lysable by this bacteriophage were considered satisfactory for use. Local applications to open lesions, subcutaneous injections and injections into and around the lesions were used. Only the cases of acne vulgaris and some of those of sycosis vulgaris did not show improvement. The patients with furunculosis, abscess, carbunculosis and mild secondary cutaneous infections were mostly all cured; the rest were improved. A few reactions were noted, both local and general. All cases showed immediate improvement after the reactions.

HENNING, Iowa City.

MULTIPLE DISSEMINATED ANGIOMAS: REPORT OF A CASE. C. J. LUNSFORD, Arch. Dermat. & Syph. **25**:344 (Feb.) 1932.

The author reports a case of multiple angiomas in a baby in which approximately 834 lesions were present. These were sharply circumscribed, slightly raised, red and variously shaped, and varied in size from that of a pinhead to that of a dime. Distribution over the body was general. The lesions were successfully treated with carbon dioxide snow. Therapy with radium was shown to be impracticable in the presence of so great a number of lesions. From twenty to thirty seconds' application of a pencil form of carbon dioxide snow gave the best results. An examination three years after treatment showed a clear skin without abnormalities.

HENNING, Iowa City.

PERSISTENT NODULES IN SCABIES: HISTOLOGIC OBSERVATIONS AND TREATMENTS. SAMUEL AYRES, JR., and NELSON P. ANDERSON, Arch. Dermat. & Syph. **25**:485 (March) 1932.

The authors wish to call attention to a complication of scabies consisting of the occurrence and persistence, after thorough treatment, of pruritic, pea-sized, nodular lesions. The nodules occurred in five cases observed over a period of one and one-half years. These pea-sized nodules were red or brownish red and were always definitely infiltrated. In all cases they were intensely pruritic. The nodules appeared most commonly on the buttocks, penis and anterior axillary folds. Histopathologic changes in two cases consisted of a marked perivascular cellular lymphocytic infiltration in the midcutis and deep cutis. No parasites, larvae, eggs

or fecal material were identified in any of the sections. The question was asked as to the possible etiology of these nodules. Electrodesiccation or coagulation followed by curettement seems to be the treatment of choice.

HENNING, Iowa City.

MILROY'S DISEASE. GARRY R. BURKE, M. J. & Rec. **135**:107 (Feb. 3) 1932.

The author reports a case of Milroy's disease in a girl, aged 18. Her complaint was persistent edema of the legs and arms, with recurrent attacks of pain accompanied by severe fever and prostration. Eight years previously she had noticed a scratch on her right ankle which became very red. The redness extended to the foot, and swelling ensued, accompanied by a high temperature and malaise.

The attack subsided but the swelling remained. During the next four years, these acute attacks recurred about every six months in the legs and arms. The leg became so large that a Kondoleon operation was done on both sides of the right leg. The size of the leg was not reduced by the operation. The attack in the arms usually came on without apparent injury.

An aunt of the patient was reported to have a similar condition. The physical examination of the patient gave negative results, except that during an acute attack the white cell count rose to 37,500 with 93 per cent polymorphonuclear neutrophils and 6 per cent small lymphocytes. The blood of the mother, brother and sister was examined at night for microfilaria. All the specimens were negative. The familial factor in Milroy's disease was not found in this case except for a suggestive history in an aunt living in Europe.

WILLIAMSON, New Orleans.

ECZEMA IN INFANCY AND CHILDHOOD: ITS RELATION TO ALLERGY. LEE BIVINGS, South. M. J. **25**:223 (March) 1932.

The author is of the opinion that most infantile eczemas are allergic in origin. Prompt and lasting relief can usually be obtained by thorough testing and the elimination of offending foods. Cow's milk, eggs and wheat are the most common offenders, but other foods must also be considered. Local treatment, combined with testing and elimination, is probably the best method for success.

SCHLUTZ, Chicago.

EXPERIMENTAL INVESTIGATIONS OF THE CUTANEOUS CHANGES IN EXTERNAL AND INTERNAL CHRONIC THALLIUM POISONING. A. BUSCHKE and J. VON VÁSÁRHELYI, Dermat. Ztschr. **63**:37 (Jan.) 1932.

As a result of experiments carried out on rats, mice and monkeys, the authors show that local applications of thallium cause generalized alopecia and slight inflammatory changes similar to those caused by the internal administration of the drug. Local alopecia appears before the generalized falling out of the hair when the thallium is applied locally. The action of the drug is explained on the basis of the effect on the nerve endings.

TAUSSIG, San Francisco. [ARCH. DERMAT. &. SYPH.]

Surgery and Orthopedics

UMBILICAL HERNIA. RICHARD H. MILLER, New England J. Med. **206**:389 (Feb. 25) 1932.

In the past ten years (from 1921 to 1930) 223 patients were admitted to the Massachusetts General Hospital and operated on. Of these, 185 (83 per cent) had simple umbilical hernias and 38 (17 per cent) strangulated umbilical hernias. In the simple cases there were 6 deaths (3 per cent), and in the strangulated cases 12 deaths (31 per cent).

While practically all of the cases were in adults, the mortality was so high in the strangulated cases that pediatricians should realize the possible seriousness of this condition.

GENGENBACH, Denver.

OPEN REDUCTION OF CONGENITAL DISLOCATION OF THE HIP. F. C. KIDNER, South. M. J. **25**:350 (April) 1932.

The author presents a method of open reduction of congenital dislocation of the hip which seems to give favorable results in children under the age of 10 years. Reduction by this method is so stable that the time of fixation in plaster is considerably shortened. Physical therapy with passive motion can be started after six weeks, and walking has been allowed after eight weeks, although the author thinks that probably twelve weeks would be safer. The method is simple and involves a minimum of trauma. It is essentially safe, and there is little tendency to redislocation. In many cases the necessity for shelf operations is avoided. The period of convalescence is cut practically in half.

SCHLUTZ, Chicago.

ACUTE OSTEOMYELITIS. E. D. FENNER, South. M. J. **25**:355 (April) 1932.

The author points out the serious consequences of delayed diagnosis and delayed treatment in this condition. Obscure clinical findings and negative roentgenograms often contribute to this delay.

The author advises early operation over a tender spot, incision of the periosteum and drilling of a hole or several holes in the bone.

Cultures from the drill hole will sometimes show the presence of staphylococci before pus is actually formed. If pus appears in the drill holes, incision and drainage should be practiced.

SCHLUTZ, Chicago.

OSTEOMA OF THE TONGUE. DAVID M. GREIG, Edinburgh M. J. **39**:93 (Feb.) 1932.

Greig gives a critical review of the subject of osteoma of the tongue. Tumors of the tongue are rare except for carcinomas. Osteoma and its congener occurring in connective tissues, fibroma, probably always occur together. They are rare and unlikely, although in the presence of so much fibrous tissue in the tongue fibroma would be more often expected.

In the literature there are reports of two instances of removal of lingual fibroma in children. A small fibroma present from birth occurred in a 6 weeks old child. This fibroma was on the tip of the dorsum of the tongue and caused reflex vomiting when the child was lying on the back. Another tumor described by Barling came from the middle of the tongue of a child aged 1½ years.

Greig reviewed all of the twenty-nine cases. The growths began as fibromas and belong as osteomas to the congenital simple heterotopic growths. Greig cites all the references to the subject in the literature.

NEFF, Kansas City, Mo.

ACUTE ABSCESS OF THE POSTERIOR MEDIASTINUM; SURGICAL INTERVENTION AND RECOVERY. C. SALAZAR DE SOUSA, Arch. de méd. d. enf. **35**:33 (Jan.) 1932.

Suppurative processes in this area are so rare that slight mention is made of them in pediatric works. The author reports the case of a boy of 3 years, with an unimportant personal and family history, stricken with acute rhinopharyngitis, corresponding in all its characteristics to the prevailing grippal epidemic at that time encountered in Lisbon.

In the course of a few days, however, there developed a brassy cough, with hyperpyrexia, extreme prostration and fetid expectoration. As a foreign body or pulmonary abscess was suspected, roentgenograms were made, and a shadow

as large as a small plum was noted in the right mediastinum. This was interpreted as an acute abscess; exploratory puncture in the seventh interspace, a finger-breadth to the right of the spinous processes and directed outwardly, evacuated 4 cc. of thick, foul-smelling pus. Following this, 5 cg. of neoarsphenamine diluted with 2 cc. of distilled water was injected directly into the abscess cavity. This was repeated, after aspiration, two days later and again two days after that, but in spite of medical treatment the roentgenograms showed a rapid extension of the process. Surgical aid was solicited at this point; the eighth rib was resected near the spine, and ready access to the abscess secured. Drainage was followed by prompt recovery.

AMESSE, Denver.

A CASE OF MASSIVE PULMONARY SARCOMA SECONDARY TO AN OSTEOSARCOMA OF THE RIB. M. SERFATY and OSCAR R. MAROTTOLI, Arch. argent. de pediat. **2**:373 (July) 1931.

The authors report the case of a girl 8 years old who presented a fluctuant mass the size of an orange in the anterior portion of the right rib, which began insidiously four months previous to examination, the outstanding symptoms being pain in the involved region. Roentgenologically the rib was shown to be completely destroyed by the neoplasm, which proved to be an osteosarcoma.

In spite of extensive resection of the involved rib and the surrounding tissues, followed by application of deep roentgenotherapy, the patient came in again fourteen months later with marked cachexia and extensive pulmonary involvement which on autopsy proved to be due to massive pleuropulmonary small round cell sarcoma.

SCHLUTZ, Chicago.

ANATOMIC AND FUNCTIONAL LATE RESULTS OF ONE HUNDRED AND FIFTY OPERATIONS FOR CLEFT PALATE. E. PAGNAMENTA, Deutsche Ztschr. f. Chir. **235**:214, 1932.

Pagnamenta reports the results in the cases of 150 children operated on in the surgical division of the Children's Hospital of the University of Zurich, between May, 1923, and June, 1930. Two patients died following operation. Only 113 of the remainder could be followed up in a satisfactory manner.

According to the author, the Dieffenbach-Langenbeck procedure, which he did not describe, has proved the most suitable in European practice. In this series the previously known fact that cleft palate occurs chiefly in males and more frequently on the left side was confirmed. Thirty-eight and eight tenths per cent of cases occurred in first-born children. In 30.6 per cent a hereditary factor could be established. Statistics here are uncertain, because of the tendency of the condition to skip two, three or even four generations. Twenty-five per cent of the patients were estimated to have some degree of mental retardation. Thirty per cent had difficulty in hearing. This was increased to 40 per cent in cases of bilateral clefts. Two thirds of the patients were operated on before their third year of age, in most cases toward the end of their second year. This age is regarded as being more favorable to the prognosis with respect to anatomic and phonetic results than operation at a later period.

As a result of his experience the author concluded that in partial clefts (those involving only the soft palate), if no unusual difficulties are encountered in the operative procedure and healing process, and if the patient receives proper instruction in speech, a completely satisfactory result is obtained in mentally normal patients. Subtotal clefts (those involving the soft palate and the hard palate as far as the alveolar process) do not yield such good results, especially with regard to functional aspects, as a short, tense soft palate may result, oftentimes with nasal speech. In complete unilateral clefts (those involving the hard and soft palates, alveolar process and frequently the lip) the Langenbeck operation is often contraindicated and is always contraindicated in complete bilateral clefts. In these cases after-treatment with prosthesis and instruction in speech are always essential.

Anomalies of the jaw frequently develop in patients with cleft palate, and these may be made worse by the operative procedure. For this reason during the period of growth the patient should be under the care of an orthodontist. Temporary mechanical approximation of the palatine bones gives better results in bilateral clefts. Normal anatomic relations in severe cleft palates, however, cannot be restored by purely surgical methods. The optimum end-results can be obtained only by the combined efforts of the surgeon, dentist and vocal instructor.

GLASER, Rochester, N. Y.

OPERATIVE REMOVAL OF FOREIGN BODY FROM THE DUODENUM OF AN INFANT. E. MELCHIOR, Med. Klin. **27**:1891 (Dec. 24) 1931.

A 9 month old infant swallowed an open safety-pin. Removal from the esophagus by esophagoscopy was unsuccessful, and two days later roentgen examination showed the pin with the blunt end pointing downward in the region of the duodenum. Apparently the pin was caught in the descending part of the duodenum. Laparotomy was performed two days later, and the pin was removed without any further untoward effects, although a small perforation was found in the upper end of the duodenum. The author emphasizes particularly the danger of perforation due to antiperistaltic movements.

ZENTAY, St. Louis.

TRANSITORY MILD COXITIS (COXITIS FUGAX). A. COLACO BELMONTE, Nederl. tijdschr. v. geneesk. **75**:5197 (Oct. 17) 1931.

Attention is drawn to a mild, transitory form of coxitis, occurring especially in children. Differentiation of this condition from tuberculous coxitis with a severe prognosis is of special importance. Special treatment is not necessary. With rest the subjective and objective manifestations disappear in some days or weeks. An analogous clinical picture occurs in the knee joint and in spondylitis.

VAN CREVELD, Amsterdam, Holland.

Miscellaneous

WHAT CONSTITUTES A COMPLETE PEDIATRIC DEPARTMENT IN A MEDICAL SCHOOL? A. GRAEME MITCHELL, Arch. Pediat. **49**:181 (March) 1932.

The author's summary follows: "There has been no ambition to make this a conclusive presentation, but a summary shorn of detail and explanation may be justifiable. A complete pediatric department should have five functions: Investigation, undergraduate teaching, graduate teaching, care of patients and public health activities. Investigation implies research in laboratory, clinic and community. All children must be under medical care of the pediatric department; that is, they must be considered well or sick children and not surgical, neurological or laryngological cases, as the case may be. There must be interest in and contribution to public health activities, but the primary objects of the department should be the academic ones of teaching and research. The personnel should be a combination of full-time, part-time and voluntary workers, some of the full-time workers being allowed limited outside contact. The head of the pediatric department, whatever else his qualifications, should be a clinician. The facilities should comprise hospitals, outpatient clinics, laboratories and other institutions and organizations concerned with the care of the well and sick child and the teaching of preventive medicine."

WADDELL, JR., University, Va.

INFECTION AND BEHAVIOR. CLIFFORD SWEET, Arch. Pediat. **49**:190 (March) 1932.

Attention is called to behavior reactions on the part of children suffering from infections, both acute and chronic. The writer feels that sudden and otherwise

unexplained changes in temperature are frequently the result of infection, and cites certain of his cases supporting this view. Remote and indirect reactions of infection on behavior are not clearly understood, and it is to these types of behavior problems that attention is called.

WADDELL, JR., University, Va.

THE DANGER OF CHILDREN'S PARTIES. H. BROOKER MILLS, M. J. & Rec. **135**:279 (March 16) 1932.

The dangers resulting from children's parties are both physical and mental. The difference between the temperature of the house and that of the street and the exposure to colds and other infectious diseases of childhood are among the physical dangers. The restless night after the excitement of the afternoon and the fretful day following the restless night are among the mental dangers. The author suggests methods for parents to practice to prevent disease.

WILLIAMSON, New Orleans.

THE ALLERGIC CHILD. GEORGE W. BRAY, Brit. J. Child. Dis. **29**:1 (Jan.-March) 1932.

Allergic responses, when analyzed, fall into two groups: (1) hereditary predisposition and (2) acquired sensitization. During childhood, the chief etiologic factor is the hereditary tendency, which can be demonstrated in from one half to two thirds of all cases. Of the nature of this "allergic diathesis" little is known, but recent work would suggest that some biologic factor is involved.

The common characteristics of allergic conditions are considered and discussed in some detail. The difficulty that is frequently experienced of differentiating the "allergic" from the "infectious" cold is mentioned. Enuresis is cited as a common accompaniment of other allergic conditions; in some cases, it is the sole manifestation of allergy.

The treatment of the acute symptoms and the endeavor to prevent relapses by desensitization are briefly taken up.

LANGMANN, New York.

THE DENTAL PROBLEM: THE PREVENTION OF DENTAL DISEASE. J. C. M. SHAW, South African M. J. **6**:147 (March 12) 1932.

Shaw emphasizes the part that dental disease plays in the incidence of disease in general, and expresses his opinion that the average medical practitioner does not realize that many medical problems have dental disease as a contributing factor. Furthermore, he believes that the average physician does not appreciate the progress in the study of the cause of caries that has taken place and the preventive means that have become available since the beginning of the present century.

The reason for this unhappy situation is to be found in the fact that the whole picture of dental disease has been clouded by the promotion of so many erroneous theories in explanation of the prevalence of caries. Chief among these unestablished theories are those of heredity, immunity (especially racial), acidosis (Broderick), lack of phosphorus (Lennox) and lack of vitamin D (Mellanby). Of these theories, the one that has received the most attention is that of Mellanby. Objections to the Mellanby theory, that vitamin deficiency leads to the development of hyperplastic teeth, thereby predisposing the teeth to caries, are:

1. In 1897, Carpenter and Pedley investigated the possible association of dental hypoplasia, rickets and dental caries, and found that in rachitic children there is, as a rule, no deficiency of enamel, and that there is "no evidence to prove that caries is more frequent among rickety children than among those who are suffering from other diseases." At a later date, Sir Norman Bennett arrived at a similar conclusion.

2. Hypoplasia is extremely rare in temporary teeth, this fact having been shown by Pitts, who found as a result of microscopic examination of 5,000 temporary

teeth, that less than 1 per cent were affected with hypoplasia. Yet caries is even more rampant in children's first teeth than it is in the teeth of adults.

3. It is a well known clinical fact that hypoplastic teeth are particularly resistant to caries. For example, the hypoplastic Hutchinson's teeth are almost always free from caries.

4. While rickets is practically an unknown disease in Johannesburg — presumably owing to the great amount of sunshine producing an abundant supply of vitamin D by its action on exposed skin or by the exposure of the ergosterol contained in the skin — dental caries is just as common as it is in England, where the prevailing amount of sunshine is much less than in Africa.

The explanation of caries that is now generally accepted is that it is caused by the action of food in the mouth (J. Sim Wallace). "We now believe, and there is overwhelming evidence to prove, that caries is largely, if not entirely, due to the nature of our diet. We believe that the only universal cause of caries is the action of food in the mouth. Caries is a chemico-parasitical process primarily involving the fermentation of carbohydrates. What determines the production of caries (i. e., the cause of caries) is unduly prolonged lodgment of carbohydrates under conditions favourable to the production and accumulation of acid in sufficient strength to destroy the enamel. (Carbohydrates which do not lodge or ferment or cause other carbohydrates to lodge unduly do not cause caries.) Besides the bacteria which produce acid, others generally take a share in the process; for example, the bacteria which convert the disaccharides into monosaccharides, and those which cause manitic fermentation. The exciting cause (acid-forming bacteria) is primarily outside of, and altogether independent of, the histological structure of the tooth."

Predisposing causes of the present prevalence of caries are: (1) increase in the quantity of sugar consumed; (2) refinement of cereals, which results in removal of vitamins and removal of the necessity of vigorous chewing with the consequent polishing action on the teeth; (3) increase in the use of tinned foods, the processing of which also results in destruction of vitamins and in changes in the food such that it requires a minimum of chewing; (4) increase in the consumption of pastry, which, of all foods, produces acid most easily, and which mixed with saliva is peculiarly difficult to remove from the teeth, and (5) increased feeding of young children nothing but soft foods, which do away with the necessity of vigorous chewing and consequent physiologic self-cleansing of the mouth.

The ideal diet for the prevention of dental caries in children has been shown by the author and Friel, by Wheatley and by Bunting, Jany and Hard to be one that is well balanced, plentifully supplied with detergent food, and limited in sugar except so far as necessary to make the food palatable. The dental profession being inappropriately placed for the dissemination of information directly to those most concerned with the prevention of dental caries, it is up to the medical profession to learn the elements of oral hygiene, and having learned these, to teach them to their patients, to teachers in schools and to public health authorities. The medical profession will have to learn that sugar is the arch demon of decay, and that an increased consumption of detergent foods and a decrease in the consumption of foods of the fermenting type are the only means whereby dental disease will be eradicated.

GONCE, Madison, Wis.

PLACEMENT OF DELINQUENT CHILDREN IN PRIVATE FOSTER HOMES. H. WEISS, Rev. internat. de l'enf. **12**:275 (Nov.-Dec.) 1931.

As a late probation officer of the Boston Juvenile Court who is now an officer of the International Migration Service of the League of Nations, Weiss speaks on this sociologic problem with considerable authority. It would appear that, while the placing of normal children in foster homes, rather than in institutions, has deservedly gained in favor throughout the world, the care and education of delinquents have almost by common consent been allocated to correctional schools.

This disposition of the problem, the author avers, is unjust and archaic; if the normal child needs the counsel and advice of a family where he is welcomed as a member of the household, how much greater is the need of one socially, mentally and emotionally handicapped?

Aside from a few exceptions, the institution is yet to be created which can adequately meet the needs of the juvenile court child; group handling should be employed only as a last resort when all other measures fail.

AMESSE, Denver.

HOSTELS FOR THE YOUNG IN GERMANY AND OTHER LANDS. B. NEINDORF, Rev. internat. de l'enf. **12**:291 (Nov.-Dec.) 1931.

Beginning in a small way as early as 1884, the youth movement has extended in Germany, particularly since the war, until at present there are 26 regional organizations, 1,000 local groups and 100,000 members, while its 2,200 hostels or inns registered in 1930 over 4,000,000 admissions for a night's lodging.

This spontaneous *Wandervogel* activity does not exist to any great extent in other countries of Europe, although the boy scout camps of England and America correspond to it in a measure. The hostels encourage young people in general to develop a love for out-of-door life and for expeditions and excursions; the whole idea seems to have captured the imagination of German youths, who seem to be profiting immensely through its judicious exploitation.

AMESSE, Denver.

INFANT WELFARE IN GREECE. S. VERAS, Rev. internat. de l'enf. **12**:308 (Nov.-Dec.) 1931.

Infant mortality is still inexcusably high throughout Greece, varying between 163 and 229 per thousand live births. A strong movement is now under way to correct this deplorable situation; welfare clinics are being established in the larger towns where the percentage of losses is greater than in the country districts. In explanation of this apparently paradoxical report, it is stated that breast feeding is almost universal among the rural population. The campaign for better housing, for the education of public health nurses, for vaccination with B C G. and for the financing of milk depots constitutes an interesting reflection of the awakened health consciousness.

AMESSE, Denver.

ANAPHYLAXIS AND THE CURE OF ANAPHYLAXIS. T. GUGLIELMINI, Prat. pediat. **10**:67 (Feb.) 1932.

Dr. Guglielmini briefly reviews the criteria for the diagnosis of the anaphylactic state and discusses therapeutic methods, giving a good bibliography of the Italian literature on the subject.

DOOLEY, Kent, Conn.

INFANT MORTALITY IN SÃO PAULO. WALDOMIRO DE OLIVEIRA, Bol. Inst. internac. am. de protec. a la infancia **5**:280 (Jan.) 1932.

The birth rate in São Paulo was 31.26 per thousand of population for the five year period from 1925 to 1929. Stillbirths in São Paulo in 1929 were 1.73 per thousand of population and 56.51 per thousand of total births. Syphilis was responsible for 60 per cent of the cases of stillbirth, but the campaign carried on against this evil has been particularly successful in the districts where sanitary measures are employed, and after five years the improvement in the different districts reached 15.51 and even 16.82 per thousand. The infant mortality in 1928 was lower in São Paulo than in the other capital cities of the country, but higher than in many foreign cities. The mortality increases during the months from September to December, the changes of temperature and the degree of atmospheric moisture acting either directly on the human body or indirectly

through the increase of bacteria in substances that produce digestive troubles. As to the causes of the mortality, nothing may be conclusively said as yet, owing to the number of cases in which the word "undetermined" accompanies the registration statements. These cases represented 59.78 per cent of the total in 1929, and 61.54 per cent in the five years from 1925 to 1929. The figures for diarrhea and enteritis are very high, and it would be preferable to include all the cases of these conditions under the common heading of "digestive and other troubles derived from nutrition"; the diseases of the respiratory system give a high though not an exact percentage, since many of the cases of these diseases are included under other headings.

EDITOR'S SUMMARY.

PATHOLOGIC PHYSIOLOGY OF PRIMARY DENTITION. J. M. CLUET GARCIA, But. Soc. catalana de pediat. **1**:27 (Oct.) 1928.

The process of primary dentition was followed carefully in sixty-two cases over a period of four years. The results revealed that a marked retardation in the time of eruption is almost always due to rickets, while alteration in the order of appearance of the teeth is usually accompanied by a retardation. In normal dentition there are a retardation in weight and height, anorexia, slight nervousness, increased vagotonia and decreased resistance. Difficult dentition is nothing more than an exaggeration of what occurs in normal dentition. Dentition itself is incapable of producing any disease, but both normal and difficult dentition may aggravate existing pathologic conditions by producing hypervagotonia or decreasing resistance.

WATSON, Elmhurst, Ill.

THE VALUATION OF THE RESULTS OF VACATIONS AND REST CURES. ELFRIEDE GOLKE and FRANZ HEIMANN, Gesundhfürs. f. d. Kindesalt. **7**:15 (Feb.) 1932.

This article is chiefly of value in showing the social conditions at present prevailing in Germany and the serious effect on the children. The authors show how difficult it is to obtain permanent results since the children return to homes in which the greatest privation reigns.

REICHLE, Cleveland.

EARLY INFANT MORTALITY. JOSEPH KOHN, Gesundhfürs. f. d. Kindesalt. **7**:42 (Feb.) 1932.

This is a discussion of statistics obtained from the Women's Hospital in Berlin. With the exception of stillbirths, early mortality does not play a great rôle in the total infant mortality.

REICHLE, Cleveland.

THE PHYSICAL AND MENTAL CAPACITY OF THE SCHOOL CHILD IN RELATION TO ITS CONSTITUTION. ELSE LIEFMANN, Monatschr. f. Kinderh. **52**:305, 1932.

Dr. Liefmann was in charge of a school in which the children fell into three groups: Thirty-three were talented, sixty-six were mediocre, and thirty-three were definitely retarded. In an effort to correlate mental and physical development, she measured the height, weight, chest circumference, respiratory excursions and lung capacity. Without any question, the mentally alert children showed themselves superior in all these physical measurements.

Investigation of the home conditions showed the same situation; the brighter children came from superior economic and social environment.

The third part of the study consisted of certain types of physical exercise, such as balancing, running and jumping. Here it was a little harder to reach the same conclusion, as the factor of weight played a part, the lower weight being an asset in some of the exercises. However, as a general average, the mentally superior children also excelled in the various exercises.

The suggestion is offered that the types of exercise given to the subnormal child should be different from those given to the normal one.

GERSTLEY, Chicago.

FORTY-SECOND SESSION OF THE GERMAN PEDIÄTRIC SOCIETY. Monatschr. f. Kinderh. **51**:321 (Feb.); **53**:1 (April) 1932.

The meeting was held in Dresden from Sept. 23 to 26, 1931. The first session's program, on September 24, was devoted mainly to disturbances of the nervous system. Questions of the physiology of sex were discussed in the usual fashion and were more or less incomprehensible to the average pediatrician. Following these reviews by Goett and Friedjung, Boenheim introduced some interesting observations in a study of masturbation. He compared the environment of children who masturbated excessively with the environment of children who had other nervous stigmas, such as chorea and tic. While the children with chorea, tic and enuresis seemed to come from families in which there was definite nervous disease, in the families of the children who masturbated, almost 100 per cent of the histories showed unhappiness and sexual abnormalities such as prostitution.

Doxiades, in muscular tracings, demonstrated some differences between the tone of skeletal muscle in patients with chorea compared with normal persons, as well as some interference in the reciprocal relations between antagonists, and Lenart argued that chorea was an endocrine disturbance. Knauer studied the lipoids in spinal fluid and blood, finding no relationship.

The second session was given to a consideration of metabolism. Fasold demonstrated that the addition of sodium chloride to breast milk had little effect on the excretion of bicarbonate and ammonia in the urine. When added to lactic acid milk it caused an enormous increase in the excretion of ammonia and bicarbonate. Mommsen and Eitz offered evidence to show that the milk of menstruating women contains toxic substances. These observations stimulated considerable discussion and criticism. An interesting paper was presented by Kerpel-Fronius. He showed that the kidneys of a new-born infant are incapable of effecting a marked increase in the concentration of urine. This faculty does not develop until after the first few months. It is for this reason that the younger children require such large quantities of water in proportion to their body weight. Rosenbaum of Leipzig introduced experimental evidence to show that the deep breathing in alimentary intoxication is not necessarily due to an increased hydrogen ion concentration of the spinal fluid and blood.

Paffrath and Massert presented conclusions differing from other experimenters in regard to parallelism of salt and water retention. These observers support the original idea that the two substances are retained and excreted in parallel in premature infants. Beck, in studying the iron metabolism of premature children, showed that the greatest loss occurred from the thirtieth to the fortieth day. Feeding iron caused some retention, but this was all excreted again following cessation of the intake.

The third session was given entirely to a consideration of diphtheria. The Germans do not have the same faith in the routine immunization against diphtheria that physicians have in the United States. A number of observers reported results that were not convincing as regards the efficiency of the routine preventive inoculations. Schick read a splendid paper arguing for the measure and quoting the good results obtained in this country.

Bruhl, noting the increased frequency of respiration in children with tetany, studied the carbon dioxide content and the hydrogen ion concentration of the venous and the arterial blood. He found that in normal children the curves of the venous and arterial blood are superimposed, and that in children verging on tetany there is a definite difference. He also discovered that ultraviolet irradiation led to curves resembling those of tetany, and suggests that this may explain the exaggeration of symptoms in the early spring. Catel reported studies comparing raw and autoclaved milk. He concluded that raw milk is far superior in

animal experimentation, and confirmed clinical observations with metabolic experiments. Keller, with the Prausnitz-Küstner reaction, showed that from 0.05 to 0.1 cc. of egg-white introduced into the stomach of an infant will give a positive cutaneous reaction in three minutes.

Klinke suggested that in the vomiting of so-called "acidosis," the loss of hydrochloric acid may play a part, and he claimed good results from giving these children 5 drops of hydrochloric acid in water at frequent intervals. Much discussion followed this paper, most of which suggested that the work was unconvincing. Gravinghoff believes that one can make a prognosis of tuberculosis by combinations of blood examinations, using the Arneth, Schilling, Helmreich and supravital methods. This seems rather cumbersome. Wiese gets satisfactory results in the treatment of bronchiectasis by making an incision over the affected area and then forcing in sufficient inert substance extrapleurally to collapse the cavities. Klinke, with Hensel, introduced a new serodiagnostic test for active tuberculosis based on changes in the blood colloids. Weiss discussed nephritis in congenital syphilis, saying that it was frequently associated with hematuria, leukocytes and casts, and was of extremely grave significance.

Abels ended the session in a discussion of the habitus asthenicus, in which he called to mind the fact that this is not simply a condition of the osseous system but is a constitutional anomaly affecting the muscles, the organs of the body and the resistance of the body to infections, particularly tuberculosis.

GERSTLEY, Chicago.

PROCEEDINGS OF THE GERMAN PEDIATRIC SOCIETY (CONTINUED). Monatschr. f. Kinderh. **52**:334, 1932.

The third session proceeded with a paper by Paul von Kiss, who demonstrated interesting electrocardiograms taken in cases of diphtheria. He cited cases of sudden death in which the physical examination had revealed a normal heart and vice versa. He concluded that an appraisal of the patient's heart during severe diphtheria must include an electrocardiogram.

Claus Jensen reported interesting studies on the Schick reaction, showing that sometimes a negative Schick result is obtained while the patient is still susceptible to diphtheria. The assembly then reopened the discussion on diphtheria, particularly with reference to immunization. At this time, the majority of observers seemed to favor the procedure, with the exception of Schlossmann, who, in a surprisingly rude and tactless onslaught against the paper of Schick, showed himself no longer in sympathy with modern pediatrics.

The fourth session was opened by St. Engel, who believed that the importance of the excessive mucosa in pyloric stenosis had been underemphasized in comparison with the musculature. Samson reported determinations of albumin in the spinal fluid in cases of meningismus. In pneumonias with this symptom, the albumin in the spinal fluid is diminished, and Samson believes that the increased water from the spinal fluid is responsible for the meningeal symptoms. Leitner obtained good results with ethylhydrocupreine in pneumonia. Kurt Scheer showed that in glandular fever the blood count of infants differs from that of adults in showing an increase in the number of polymorphonuclears. Bayer discussed recurrences in whooping cough, reporting them as very rare. Redlich cited an interesting case in which a vaccination for smallpox seemed to sensitize a child to streptococcic sepsis. Becker produced blisters with cantharides and found the white cells in the blister fluid showing the same proportions as in the blood. Joachims fed children diets deficient in water and produced desiccation fever, cured it by addition of water and studied the water and protein content of the blood during the procedure. Rominger and Meyer used the newer cardiologic instruments and showed the differences between the pulse curves of infants and adults. In the infant, systole consumes 41 per cent of the cardiac cycle against 30 per cent in the adult. The blood flow is also somewhat slower in the infant. Seckel, reporting on orthostatic albuminuria, described associated symptoms, which he

believes to be due to vasomotor disturbance; he suggested that the name be changed to "orthostatic vasoneurosis." Nobel cited three cases of Basedow's disease in children. Treatment with x-rays plus high caloric diet proved effective. Bischoff reported measurements of the esophagus, and Viethen briefly discussed intravenous urography.

The fifth session opened with interesting studies by zu Horste on the effect of different substances on calcification in test tube experiments. Small amounts of glycogen and dextrose cause definite inhibition of calcification of tissues in vitro. Lactic acid had surprisingly little effect. Stettner showed that x-ray pictures of the bones of infants and children normally show osteoporosis compared with those of adults. Gerstenberger and Horesch treated infants with a new electric ultraviolet ray lamp and reported it to be satisfactory. Nitschke, Koch, Maier and Schmidt isolated two substances from the lymph. One seems to be a factor in causing infantile tetany; the second leads to diminution of inorganic phosphorus in the blood serum. Simultaneous changes were noted in the thyroid gland.

GERSTLEY, Chicago.

THE INFLUENCE OF HOT WEATHER ON ATROPINIZED INFANTS. HANS SCHMIDT, Monatschr. f. Kinderh. **53**:125, 1932.

Four infants were treated with atropine for pyloric stenosis. During the treatment a period of hot weather occurred. On the hot days the infants' temperatures varied from 38.9 to 41.5 C. (102 to 106.7 F.). The association of the hot weather with the fever leads the author to place the blame on the atropine. There was no injury from the hyperthermia, and one patient seemed improved.

GERSTLEY, Chicago.

IMPORTANCE OF KNOWLEDGE OF THE FAMILY BACKGROUND. CARL COERPER, Monatschr. f. Kinderh. **54**:316, 1932.

All pediatricians realize the importance of knowledge of the family background of the patient. Many believe this to be almost exclusively a knowledge of the heredity. However, of equal importance is a knowledge of the health education of the child and a knowledge of the social environment.

The development of constitutional clinics in the future may center less around the sick children's clinic and more around the welfare stations.

GERSTLEY, Chicago.

RECTAL ADMINISTRATION OF BLOOD PLASMA IN INFANTS. E. GYÖRGY, Monatschr. f. Kinderh. **54**:377, 1932.

There are occasions when blood therapy is indicated but when it is inadvisable to administer it parenterally, as in weak premature infants or in infants with diffuse conditions of the skin. The author attempted to give blood plasma rectally; 115 treatments were given to 25 nurslings. The material selected was of three types, premature infants with catarrhal and grippal infections, nurslings with severe cutaneous disturbances and premature infants suffering from debility. The plasma was given in doses of from 10 to 20 cc. The treatment may be repeated daily for from five to ten days.

The results were particularly satisfactory in the premature infants with grippal infections, but the treatment seemed to be helpful in all cases.

Control experiments showed serologically that the plasma was absorbed into the system.

GERSTLEY, Chicago.

CHANGES IN THE LEUKOCYTE COUNT PRODUCED BY RAYS OF VARIOUS WAVELENGTHS. H. KÜSTNER, G. DREYER and W. SEIDE, München. med. Wchnschr. **79**:703 (April 29) 1932.

The authors observed the effect of exposure to infra-red rays on white blood cells of animals and human beings. Patients were exposed to the infra-red rays on three successive days. The blood cells were counted immediately before and after irradiation, and again eight hours later. In many cases there was an increase in the number of lymphocytes and monocytes following irradiation. Guinea-pigs also showed an increase in the lymphocytic cells following exposure to the red light rays. On the other hand, exposure to blue light rays counteracted the lymphocytosis and produced a leukocytosis. The reaction of the blood was not influenced by the administration of ovarian hormone.

BRAHDY, Mount Vernon, N. Y.

DANGERS OF OVERDOSAGE OF GRENZ-RAYS ON THE GROWING ORGANISM. M. KOLREP, Ztschr. f. Kinderh. **53**:121, 1932.

The object of the study was to determine the effects of grenz rays on the growing organism. Since their use is spreading rapidly as a therapeutic agent in the dermatoses, such knowledge is of importance. Grenz or "limit" rays are long wave, soft roentgen rays with a wave length of about 1 to 2 angstroms, and lie between the "limits" of roentgen rays and short wave ultraviolet rays. The effects of the rays were studied on the bones of growing rabbits and rats, one leg being exposed and the other serving as a control. In rabbits 4,500 roentgens during a period of nine weeks produced no shortening of the bones. In rats the same dose produced a slight but definite shortening of the bones; 1,000 roentgens produced a marked effect. In both rabbits and rats temporary epilation was produced when the dosage reached 1,500 roentgens.

SHELLING, Baltimore.

CLINICAL DISEASE FORMS IN THEIR RELATION TO HIGHER AGES OF THE PARENTS: A STATISTICAL STUDY. C. BENNHOLDT-THOMSEN, Ztschr. f. Kinderh. **53**:181, 1932.

A statistical correlation between the age of the parents at the time of the birth of the child and tendencies toward certain diseases was made. The study was based on 13,516 case histories. In children born when the mother was 40 years of age or more, there is a tendency to mongolism and, to a lesser extent, to other cerebral diseases. There is no correlation between the tendency toward disease and (1) the higher age of the father, (2) the higher age of both parents or (3) differences in parental ages.

SHELLING, Baltimore.

Society Transactions

CENTRAL STATES PEDIATRIC SOCIETY

Seventeenth Annual Meeting, Oct. 7 and 8, 1932

Friday Morning, Oct. 7, 1932

FRANK C. NEFF, M.D., *President, Presiding*

UNUSUAL FEATURES OF ENCEPHALITIS COMPLICATING MEASLES. DR. JOHN AULL, Kansas City, Mo.

On Jan. 10, 1929, at 10 years of age, four days after the onset of measles, the patient shown by Dr. Aull went into a severe convulsion, which lasted intermittently for several hours. Her temperature reached 105 F.; she had a pulse rate above 180 and a respiratory rate of 90. The temperature gradually subsided, and reached normal on the fourth day. For three or four days afterward, she was in a semiconscious condition. Her urine showed 3 plus albumin. Chemical analysis of her blood gave negative results. A spinal puncture made on the first day showed 8 cells per cubic millimeter, with a faintly positive globulin reaction. There were no motor disturbances, except incontinence of urine, which lasted for nineteen days and which was probably due to a disturbance of the higher center of control. Ten days later she looked at the comic paper upside down. Thirteen days later she was unable to recognize her playmates. She did not know her mother until after two weeks, and was unable to recognize her school teacher, even later. Seventeen days following the convulsion, the patient was shown a match, a key and a pencil. She was unable to identify them by feeling. When asked the question, "what do you do with a pencil," she said, "strike it," but when handed the pencil, she was able to write her name. When shown pictures of large animals in colors, she was able to identify the colors, but did not recognize the forms. She did not recognize her own photograph. Reading readily came back to her, but at first she had difficulty in finding the line and in reading from the right page. One month later she put on her bathrobe backward, and she had been somewhat confused in this respect even to the time of presentation, more than three years later. One year after her sick spell she went to a party and thought that the ice cream was butter. At the time of presentation, her grades in reading and history at school were good, while those in spelling and writing were inferior. On April 28, 1925, before her illness, her intelligence quotient was 116.4, and on Sept. 28, 1932, three years following her illness, it was 114, virtually the same. According to the new Stanford achievement test, on September 28, at 12 years of age, she had a grade standing of 9.2 in the Kansas City high schools, which is an education age of 15 years and 2 months. She was in junior high school. She thoroughly enjoyed Latin, but was having difficulty with geometric figures.

THE EARLY AND LATE TREATMENT OF THE BURNED CHILD. DR. EARL C. PADGETT, Kansas City, Mo.

Generally speaking, fixing preparations such as tannic acid allow one to handle the local lesion of a burn by a sort of "let alone" method, and to concentrate on the systemic treatment, which at first is most important. The work of Underhill and Blalock has taught one that the secondary shock syndrome is due to a loss of blood plasma from the "circulatory tree," and that this loss is sufficient to cause death. In a burn of one sixth of the body surface, the loss from the "circulatory

tree" may be as much as 70 per cent of the total blood volume in the first twenty-four hours. Consequently, a transfusion of blood to replace the proteins of the blood plasma and intravenous injections of isotonic salt in large amounts are indicated, the hemoglobin and red cell count (repeatedly taken) being used as an index to keep the blood concentration within normal limits. Later—within from twelve to eighteen days—when a line of demarcation begins to form between the dead tissue and the wall of live granulation tissue, the application of gauze continually saturated in saline aids separation of the slough and prepares the granulation tissue base for skin grafting. In some cases actual soaks in a tub of saline solution may be necessary and advisable. By such a procedure a minimum amount of pain, the least mortality, the least permanent disability and, last but not least, a minimum period of convalescence are the rule. All but the most severe burns should be healed and the patient out of the hospital within from four to six weeks.

Healed cicatricial contractures are usually best treated by cross-cutting of the cicatrix, overcorrection of the deformity and application of a full thickness skin graft, which, within its proper indications, gives a good appearance, a minimum secondary contracture and a maximal functional result.

TUMORS IN THE POSTERIOR FOSSA OF CHILDREN. DR. FRANK R. TEACHENOR, Kansas City, Mo.

Dr. Teachenor presented a clinical discussion of the diagnosis and treatment of certain tumors of the brain, with results in two children, who were shown to the society.

SICKLE CELL ANEMIA IN CHILDHOOD. DR. C. G. LEITCH, Kansas City, Mo.

A brief historic review of sickle cell anemia was presented, extending from its original description by Dr. Herrick to the most recent reports of cases. The differential diagnosis between sickle cell anemia and sicklemia was discussed, together with the clinical findings in cases as presented in adults and in children.

The laboratory findings in sickle cell anemia were presented, with a demonstration of smears by lantern slides; the skeletal findings occurring in this condition were demonstrated by roentgenograms. Theories as to the cause of sickle cell anemia were presented briefly.

A colored patient with sickle cell anemia was presented, together with her three children, none of whom showed clinical, laboratory or roentgen findings of sickle cell anemia. A careful study was made by laboratory methods.

THE THERAPEUTIC ASPECT OF ENCEPHALOGRAPHY IN CHILDREN. DR. MARVIN L. BILLS and DR. HUGH L. DWYER, Kansas City, Mo.

The diagnostic value of encephalography prompted the use of this procedure in children with evident fixed lesions of the brain, such as cerebral atrophy from injury at birth, hydrocephalus and idiopathic epilepsy that failed to yield to treatment, and in one case of petit mal with mental deficiency presenting multiple developmental defects.

Although the encephalograms were made primarily to detect anatomic or pathologic abnormalities in the fluid pathways of the brain, there has been a remarkable subsidence of convulsive attacks in some cases. Several children were presented, who, having had grand mal attacks, had been completely relieved after the injection of air without other treatment.

In an infant with several deformities of the skeleton convulsions occurred on the second day of life. At 18 months of age he was unable to sit alone; he had had from thirty to forty petit mal attacks each day, and he manifested signs of intracranial pressure by constantly placing his hands to his head, extreme restlessness, irritability and mental inferiority. Encephalograms revealed cortical atrophy over one hemisphere, and the procedure was followed by marked improvement in the general condition. The cerebrospinal fluid was replaced by air four

times during the following four months and had brought about a complete cessation of seizures and a remarkable improvement in mental development.

PROBABLE PAROXYSMAL METHEMOGLOBINURIA. DR. DONALD N. MEDEARIS, Kansas City, Kan.

The patient in the case reported had had one typical paroxysm during which bloody looking urine was found to contain no cells, but gave a positive spectroscopic reaction for methemoglobin and oxyhemoglobin. During the paroxysm the Wassermann reaction of the blood was positive. A positive serology was also present in the father. There was a definite depression in the number of platelets during the attack. The anemia at that time was severe, but disappeared following a blood transfusion. There had not yet been an opportunity to check the Donath-Landsteiner chilling test to determine the presence of a specific autohemolysin in the patient's serum.

Dr. Medearis also showed slides of a case of spina bifida with prolapse of the uterus from the vagina and with other deformities in a new-born colored infant. The low dorsal meningocele ruptured at 3 months of age, following which death occurred from purulent meningitis. The child had bilateral talipes, umbilical hernia and prolapse of the rectum; during the course of the three months of life, hydrocephalus became more evident.

RENAL FUNCTION TESTS IN CHILDREN. DR. NELSE F. OCKERBLAD and DR. EUGENE SCHWARTZ, Kansas City, Mo.

Ten or eleven years ago Dr. Ockerblad began to experiment with the application of Major's renal function test, using creatinine intravenously as a test of the renal excretion. This work led to a number of interesting observations and also to some speculations as to the exact physiology of the excretion of certain products in the blood stream by the kidneys. It was found, after several thousand tests had been made, that the excretion of creatinine practically paralleled the output of phenolsulphonphthalein except that it seemed that the renal function test with creatinine, as suggested by Ralph Major, had a considerable value in cases of nephritis in which the phenolsulphonphthalein passed so readily that it gave no indication of the damage done to the kidney. The authors are of the opinion that the creatinine sometimes reveals cases that are missed when phenolsulphonphthalein is used. E. K. Shaw, in 1925, was one of the first to demonstrate the value of fractional renal function tests. His studies were based on forty-four tests and constitute a classic. However, none of these studies was made on children. Mendel investigated renal function in children; he did not use any dye products, but depended wholly on the determination of the blood chlorides and nonprotein nitrogen both in healthy and in sick children. In 1922, Stransky and Kochmann published some studies on renal function tests in infants, which were based entirely on the elimination of water from the kidneys. These authors did not use any of the dye substances to check the elimination tests. Griffith and Mitchell believed that the normal values for the urinary excretion of phenolsulphonphthalein in children were practically the same as those for adults. Rowntree and Geraghty, in 1909, published their monumental work on phenolsulphonphthalein as a test of renal function and laid down the one hour, two hour basis, which remained a standard until Shaw, in 1925, pointed out that the fifteen minute fractions were much more valuable. Shaw also demonstrated in the forty-four tests he made that the average normal pair of kidneys excretes 40 per cent of the sulphonphthalein in the first fifteen minutes, 17 per cent in the second, 8 per cent in the third and about 4 per cent in the fourth. The presenters' studies were carried out on children from 4 to 13 years of age. It was found that there was a considerable difference between the intramuscular administration of phenolsulphonphthalein and the intravenous method. An average of forty-four intravenous tests made on children from 4 to 13 years of age gave the following results: 39.4 per cent in the first fifteen minutes, 23.6 per cent in the second, 12 per cent in the third and 6.9 per cent in the fourth, the peak, of course, being in the first fifteen minutes

and then following the rule given by Shaw in his experimental work. The intramuscular method with fifteen minute fractions, however, gave considerably different results in twenty-four patients of the same ages as those in the previous group. The results were as follows: For the first fifteen minutes, 13.9 per cent of dye was excreted; for the second, 23.8 per cent; for the third, 23.3 per cent, and for the fourth, 13.7 per cent. At the end of the hour, practically the same amount had been eliminated with the intravenous method; however, the peak of the excretion appeared in the second and third fifteen minutes about equally, whereas with the intravenous method the peak is always in the first fifteen minutes in normal excretion. The presenters summarized their work on the excretion test as follows: Phenolsulphonphthalein is the best of the excretion tests. The intravenous method with fifteen minute fractions is by far the most valuable. When the dye is given intramuscularly, the peak is in the second and third periods. The usual two hour basis gives unreliable information. In infants the tests are extremely difficult. Every child with pyuria should undergo a test on the intravenous fifteen minute basis. Intravenous creatinine tests give no additional information. The excretion values are the same for children as for adults. The values found with the intravenous method were as follows: 39.4 per cent for the first fifteen minutes, 23.6 per cent for the second, 12 per cent for the third and 6.9 per cent for the fourth. Elimination tests on children with dyes indicate that the excretion values are practically the same as for adults.

PECULIARITIES OF PATHOLOGY IN INFANCY AND IN CHILDHOOD. DR. H. R. WAHL and DR. WARD SUMMERVILLE, Kansas City, Kan.

The pathologic reactions in infancy and childhood are similar to those in the adult, though the younger the child, the more frequent are certain peculiarities found. There is often a striking discrepancy between the functional disturbances and the anatomic findings, as, for example, the negative findings found post mortem in many cases of fatal diarrhea. Lesions in infancy are often related to defects in development, e. g., spina bifida. Gastro-intestinal disturbances are often the result of delayed and defective development of the secretory glands of the gastro-intestinal tract. Other lesions result from nutritional defects, such as a diet deficient in one of the vitamins, causing infantile scurvy or rickets.

The long bones of infants and children are much more susceptible to infections than those of adults. The same is true of the peritoneum. Enlargement of the lymph nodes is very common. Infections of the lung are commonly of the interstitial type. Nephritis in infants is frequently overlooked and often shows unusual deposits of calcium salts, suggesting the instability of calcium metabolism in infants.

AN UNUSUAL CASE OF ALBINISM. DR. ALBERT A. GAUSZ, Kansas City, Mo.

A Negro family was presented in order to show the contrast between its black members and the patient, who was a typical African albino. Partial albinism is said to be endemic in Africa and may be hereditary. In a circus recently visiting this city, there were two members of the side show who were partial Negro albinos and were said to be brothers. Although the manifestation may be more common in the Negro race, the contrast with the black members of the family makes the condition more conspicuous. The skin, hair and eyes are all typical of albinism.

THE EFFECT OF MORPHINE AND CODEINE ON THE SMALL INTESTINE. DR. HJALMAR E. CARLSON, St. Paul.

Owing probably to the general sedative effect which one obtains with morphine and codeine, it is usually assumed that the bowel also is put at rest. However, recent work has shown that the action of these drugs is one of stimulation rather than paralysis. Dr. Carlson's experiments have shown that morphine and codeine in the usual clinical doses increase intestinal tone, increase the amplitude and frequency of peristaltic waves, increase the amplitude of segmentation movements and produce a spasm of the pyloric and ileocecal sphincters.

Both clinical and experimental material was used in these experiments, and included kymographic tracings of intestinal movements obtained by the insertion of a balloon directly into the intestine in both dogs and man, the observation of large hernias and the auscultation of the abdomen before and after the hypodermic injection of morphine and codeine. Doses of morphine up to one-half grain (0.03 Gm.) were used in human beings, and an increasing degree of response was noted as the dose was increased. Experimentally, extremely large doses were necessary to stop peristalsis. The response to codeine was similar to that of morphine, except that larger doses of codeine had to be used. Further study of cases with intestinal obstruction, peritonitis and paralytic ileus by auscultation of the abdomen before and after the administration of morphine and codeine and by tracings obtained directly from the obstructed intestine in animals showed that there was little difference in response of the pathologic intestine from the normal. The effect of these drugs on the sphincters was studied by means of the barium meal in both dogs and man, and the emptying time of the stomach and small intestine was found to be delayed several hours. This is suggested as at least part of the explanation for the constipation which occurs with the use of morphine and codeine.

In the light of the newer conception of the action of these drugs on the intestine, it is concluded that further observation in children is needed to draw accurate conclusions as to the beneficial or deleterious effects which these drugs may have.

TREATMENT OF ACUTE PERITONITIS IN CHILDREN. DR. THOMAS G. ORR, Kansas City, Mo.

The mortality of acute peritonitis in children is very high. The statistics in the University of Kansas Hospital are as follows:

Number of patients, 1920-1930	29
Number of deaths	20—68% plus
Number of autopsies	17
6 patients less than 1 year of age—6 died	100%
10 patients 2-9 years of age—6 died	60%
13 patients 10-16 years of age—7 died	53%
Patients hopeless on admission, 13—13 died	100%
Patients hopeful on admission, 16—7 died	43%
In 1932, 9 patients with ruptured appendix—3 died	33.33%

This series includes diffuse peritonitis due to rupture of the intestine, intussusception with perforation, typhoid perforation, postoperative infection and ruptured appendix. A large percentage was hopeless when first seen.

The treatment now used in this hospital is outlined as follows:

1. Operation (selected cases).
2. Bed posture (head of bed elevated).
3. Morphine, codeine or a mixture of opium alkaloids and hydrochloride to keep drowsy.
4. Moist heat to abdomen.
5. Gastric or duodenal lavage and drainage.
6. Continuous venoclysis—dextrose, 10 per cent in physiologic solution of sodium chloride.
7. Proctoclysis—tap water or physiologic solution of sodium chloride.
8. Hypodermoclysis with physiologic solution of sodium chloride.
9. Enterostomy (rarely indicated).
10. Oxygen inhalation therapy.

The portion of the treatment which seems most worthy of emphasis is the proper administration of water and salt to maintain the water and chemical balance and the use of morphine in regular dosage to relieve pain, restlessness and anxiety, and to aid in maintaining the bowel tone until the infection is overcome. Dr. Carlson discussed the action of morphine on the intestinal tract. His work con-

vinces one of the usefulness of this drug in the routine treatment of peritonitis. The proper supply of sodium chloride is also worthy of special attention. Salt in suitable quantities undoubtedly is an essential factor in maintaining water and chemical balances and distribution of heat. In addition, proper salt balance apparently is a factor in restoring and maintaining bowel tone.

LACERATIONS OF CEREBRAL MEMBRANES AND BLOOD VESSELS IN THE NEWBORN. DR. WILFRED C. CURPHEY, Kansas City, Kan.

In order to study the lesions occurring as a result of trauma at birth, it is necessary to expose the dural membranes so that they may be preserved intact. This is accomplished by cutting a window in each side of the cranium and removing the brain in three sections. In this way the falx cerebri and tentorium cerebelli are preserved for examination.

After consideration of the anatomy of these structures, it becomes obvious that no matter how the shape of the head is altered the strain produced is transmitted through the membranes in such a manner that it always passes through an area in the falx cerebelli known as the "critical triangle." This area is bounded by the line of attachment of the falx cerebri and tentorium cerebelli, the free edge of the tentorium and a heavy band of fibers in the tentorium known as the "deep horizontal fibers."

Since the lines of force converge at this point and always pass through this area, it is reasonable to expect tears to occur more often at this site.

Facts confirm this theory, for in each case observed by the author the tears in the membranes were located in this region, although not always associated with hemorrhage. When hemorrhage is present, it is subdural and above the tentorium.

Predisposing factors affecting such injuries are prematurity and breech presentations.

THE IMMEDIATE CARE OF THE NEWLY BORN INFANT. DR. L. A. CALKINS, Kansas City, Mo.

If one would further reduce newly born and infant mortality, one will find great assistance in two measures now in use in the University of Kansas Hospital.

1. The proper care of the infant in the first few minutes after delivery demands maintenance of proper body temperature and avoidance of trauma. Body temperature cannot be properly maintained, particularly in the premature infant, unless the child is delivered in a room with a temperature of at least 85 F. The weak or premature infant cannot maintain his body temperature even under such conditions for a very long time and must, therefore, be promptly put beneath warmed blankets, and artificial heat must be provided in some manner. The use of hot water bottles for this purpose is entirely satisfactory. Trauma is avoided by deleting all forms of artificial respiration or "resuscitation." It is much better to use some form of respirator, employing 95 per cent oxygen and 5 per cent carbon dioxide, than it is to employ any of the older forms of resuscitation, the least dangerous of which is probably mouth-to-mouth breathing.

2. The further care of the infant is more efficiently managed by a thoroughly competent (and I would stress the words "thoroughly competent") pediatrician than by an obstetrician, whose main interest is in the mother and whose knowledge and interest in the baby are at times quite deficient. The only possible objection to the pediatrician attending the infant is failure of cooperation between the pediatrician and the obstetrician, to the end that the mother might receive advice from more than one source or that the father might be called on to pay two physicians. These two objections should, of course, be obviated in every instance. The details of the plan in each separate community are not of importance so far as the general idea is concerned.

RECOGNITION OF CATARACT IN CHILDREN. DR. E. J. CURRAN, Kansas City, Mo.

The diagnosis of cataracts in infancy is important, especially if there has been any congenital cataract in any branch of the family. As the infant's pupil is always small, it is necessary to dilate it with a small drop of 1 per cent homatropine, and then, by oblique illumination or with the ophthalmoscope, one is able to see the cataract, which may be nuclear, anterior polar, posterior polar, zonular, diffuse throughout or, more rarely, coral. These are the chief types of congenital cataract. They are not progressive. They remain the same throughout life, with the exception of the nuclear cataract, which becomes smaller.

These cataracts must not be confused with infantile cataracts, which are progressive, and which may not be congenital, although heredity plays a part just as it does in the foregoing types. This type of cataract may not be present at birth, but may appear soon afterward, and, when discovered, may wrongfully be called congenital cataract. It is the same kind of cataract as the so-called juvenile cataract, which may be delayed up to young manhood and womanhood, and even beyond.

The speaker presented a case of true nuclear congenital cataract, one of infantile cataract and one of juvenile cataract, in a man, aged 22. In a member of the latter's family, there was an infantile cataract. In another of the family, a juvenile cataract appeared at the age of 12 years. In a third member of the same family, cataracts developed at the age of 24 years; a cousin had an operation for cataracts at the age of 30 years.

These cataracts should not be confused with ordinary congenital cataracts, all of which are due to some mistake in the embryologic development of the lens.

IMPRESSIONS OBTAINED FROM THE USE OF HYPODERMOCLYSIS IN THE FIRST THREE DAYS OF LIFE. DR. E. J. SCHWARTZ, Kansas City, Mo.

In a series of unselected cases, physiologic solution of sodium chloride was given by hypodermoclysis during the first three days of life; 150 cc. was given during the first twenty-four hours, 120 cc. during the second twenty-four hours and 90 cc. during the third twenty-four hours. There were too many variables to draw any definite conclusions. However, the following impressions were gained:

1. The initial or physiologic loss of weight is markedly decreased. The return to birth weight occurred on the third day of life.

2. The intake of breast milk and water was not influenced.

3. Acute salt retention can be produced by hypodermoclysis. In one infant in the series generalized edema developed on the fourth day, and two patients had edema of one leg which persisted for forty-eight hours.

4. The average amounts of physiologic solution of sodium chloride per kilogram which are well tolerated are: 45 cc. the first twenty-four hours, 35 cc. the second twenty-four hours and 25 cc. the third twenty-four hours.

5. The most marked results were noted in babies who were born after a long labor or premature rupture of the bag of waters.

MOTTLED ENAMEL OF CHILDREN'S TEETH DUE TO THE DRINKING WATER. SELMA GOTTLIEB, PH.D., Lawrence, Kan.

The speaker took part in a survey in one of the Kansas towns where artesian water is used. Only a few communities were affected. There was a typical case in a colored child from that community in the University of Kansas Hospital at the time of the meeting, but because of an acute infection it was not deemed wise to present him to the audience. Mottled enamel is a tooth defect which first manifests itself by a chalky white, spotted appearance of the enamel instead of the normal translucent appearance. This is noticeable as soon as the tooth is erupted into the mouth. Discoloration soon occurs, and the teeth may become disfigured with areas shading from buff to dark brown.

Mottled enamel was first described about fifteen years ago, and investigations since that time have disclosed that it occurs in communities as widely scattered

as Arizona, Idaho, North Dakota and Arkansas in this country, besides Italy, Spain, Holland, Argentina, North Africa, China and various other places. In every afflicted community it has been found that the defect is associated with the common source of drinking water; practically 100 per cent of the children regularly drinking the water are affected.

Until less than a year ago, it was not known what substance in the water was causing the defect, but it is now well established that the trouble is caused by the presence in the water of relatively small amounts of the chemical element fluorine. Since the enamel of the temporary or baby teeth is formed before birth, it is rarely affected, but the enamel of the permanent teeth is formed during childhood, and is subject to harm.

The damage to the enamel is so great that dental science has as yet found no way of repairing the harm. Present evidence indicates that the affected teeth are no more liable to decay than are normal ones.

PRESENTATION OF A GROUP OF CHILDREN WITH UNUSUAL MULTIPLE CONGENITAL MALFORMATIONS. DR. FRANK C. NEFF, Kansas City, Mo.

Dr. Neff presented a number of children with congenital deformities, most of which were unusual and belonged to a hitherto undifferentiated clinical syndrome. In each of these children there was a striking abnormality of the skull or the face. On various portions of the body were other deformities, not, however, secondary to those of the head. They undoubtedly dated back to defects in the germ plasm.

Four of the children had symptoms sufficiently alike to be suggestive of a common congenital type. The children were all above average height; in some the forehead showed malformations, with a vertical metopic ridge and also a transverse furrow above each supra-orbital ridge. All had a high arched palate. Most of them had funnel-shaped chests, kyphosis, contractures of the fingers and toes and long, narrow, shapeless digits which resembled the condition known as arachnodactylia or spider fingers. In some instances there were deformities of the feet. All of these abnormalities were present at birth. There were a general muscular atrophy and relaxation resembling a congenital dystrophy. The children were all late in walking; the intelligence was retarded, but considerable general improvement had taken place. Dr. Neff had been unable to find a description of a similar syndrome. For purpose of contrast he showed one case each of true oxycephalia, pseudo-oxycephalia and the recently described syndrome of Helmholtz and Harrington, namely, "congenital cloudiness of the cornea and other anomalies." The last case shown by Dr. Neff so closely resembled those described by Helmholtz and Harrington that the child might have been mistaken for the same patient or a twin.

Friday Afternoon, Oct. 7, 1932

JULIUS H. HESS, M.D., *Vice-President, Presiding*

THE FATE OF TRAUMATIZED TEETH IN CHILDREN. A. J. HERNDON, D.D.S., Kansas City, Mo.

Traumatized teeth is a systemic condition resulting from an injury. This injury generally results from some sort of an accident, such as with a motor car, school swings, a football, a baseball, and so forth. Dr. Herndon explained the fate of these teeth if left in the mouth and the fate if removed too early in life.

CASE 1.—A boy, aged 9 years, had the four upper centrals knocked loose, two of them completely out of the socket, the result of an automobile accident. The remaining two teeth were so loose that it required careful work to make the appliance that would hold the four in place. This being done, the two centrals were pushed into the sockets, the appliance cemented in place, and the boy dismissed.

This patient was examined each day for ten days, and every three days for one month. All four teeth were found nonvital, and at the time of presentation were still what one would call dead teeth, with very little process around the centrals. Of course, from the standpoint of health, the teeth should not be left in the boy's mouth; however, he was 9 years old and no sort of an appliance could restore the front teeth, as the permanent cuspids were not yet erupted. Therefore, the teeth were to be watched until the cuspids were in place, when the traumatized teeth would be extracted and a bridge inserted.

CASE 2.—A boy, aged 9 years, had his first upper bicuspid knocked loose while playing football. When he was seen at the office, extraction of the tooth was suggested, but the mother asked that it remain and that the boy be kept under observation. One year passed before the boy returned for other work, and the mother asked that care be taken with him, as a "heart ailment" had developed.

Of course, the first thought was of the bicuspid injury, and this tooth was immediately extracted; in thirty days the boy had completely recovered. He had been able to go to school only one-half day each day, the other half being spent in bed to gain strength for the next day.

CASE 3.—A girl, aged 13 months, was thrown from her buggy. The first lower molar was knocked loose from the socket, but had remained in place seven years, when Dr. Herndon saw the patient. A chronic fistula had developed that opened under the chin, and the process was wasted away so that extraction was difficult without danger of breaking the lower jaw. This was done, however, with no serious results. The patient died two years later from cancer, the cause of which one may draw from ones own conclusions.

Dr. Herndon said that traumatized teeth can cause constant irritation, inflammation of the glands of the mouth, tumors of the jaw, extreme nervousness, malnutrition, abscesses, deformity of the mouth, irregular teeth, heart ailments, sinus trouble, rickets and arrested development of the bone structure, a harboring place for germs that will be carried into the blood stream, causing a systemic infection that could cause any of the various disorders.

In some cases, in older people, traumatized teeth are left in the mouth too long and are overused. In such cases bridges are inserted and the overuse is relieved.

THREE CASES OF TETANUS: TREATMENT WITH ANTITOXIN CONTROLLED BY AVERTIN. DR. F. A. HARRISON, Springfield, Mo.

During the fall of 1931, three patients with tetanus infection were treated in the Children's Wards of the Massachuetts General Hospital. Avertin was used in each case to control the major nervous symptoms. Its efficiency may be measured by the following summaries:

CASE 1.—A 9 year old boy entered the hospital on Aug. 29, 1931, thirteen days after a nail puncture wound. He had typical generalized muscle spasms, opisthotonos, trismus and hyperesthesia. The onset of symptoms was eleven days after the injury. On admission, he received 20,000 units of tetanus antitoxin intravenously and 20,000 units intraspinally. Two thousand units was injected into the region of the wound. Dextrose solution was given intravenously and chloral hydrate by rectum. His distress became so great twelve hours after admission that avertin (60 mg. per kilogram of body weight) was given. This quieted the child, so that he slept for some time. Within the next forty-eight hours, avertin was given on five occasions, each time bringing relief within twenty minutes, the sedative effect lasting on the average of about eight hours. After this time sedatives by mouth were sufficient. The patient was discharged in two weeks as cured. He received a total of 152,000 units of antitoxin and six administrations of avertin, with an average interval of eight hours.

CASE 2.—A 10 year old white boy entered the hospital on Sept. 8, 1931. Seven days before he had rubbed a blister on his heel, which was bandaged for two days and forgotten. There was a history of a slight pitchfork wound eight months previously, which healed quickly. On admission, the boy had marked risus sardonicus, generalized muscle spasms, opisthotonos, trismus and hyperesthesia.

Antitoxin, 20,000 units, was given intraspinally, and the same amount intravenously. A small amount was injected into the site of the wound. Fifteen hours after admission his distress was so great that avertin (60 mg. per kilogram of body weight) was administered. He was relieved for eight hours, when a second dose (80 mg. per kilogram of body weight) of avertin was given. After this time ordinary barbitals by mouth were sufficient for control. The patient was discharged twenty-three days after admission. He had received 125,000 units of antitoxin and two administrations of avertin.

CASE 3.—A 6 year old Italian boy entered the hospital on Oct. 6, 1931. For eight days he had been unable to swallow properly, and for five nights he had been restless, with mild attacks of muscle spasms. Poliomyelitis had been suspected, but lumbar puncture had given negative findings. The etiology of the infection was doubtful. He had cut his foot on a wire chicken coop several days before, and thirty-three days previously he had received a successful vaccination for smallpox. Cultures of specimens from both wounds were negative. Except for severe trismus, his symptoms were similar but milder than those in the preceding cases. Only once was avertin deemed necessary, and 75,000 units of antitoxin was given intravenously. He was discharged as cured after seventeen days in the hospital.

Avertin, or tribromethanol, needs no introduction, as there have been more than three hundred thousand cases reported in the literature within the past decade. These include every branch of medicine and surgery from ranking members of the medical profession. In the symptomatic treatment of tetanus infection, a sedative is frequently and definitely indicated. Its value is twofold: first, to reduce the reaction to stimuli which, although small, may start a tonic or clonic convulsion; secondly, to relieve the discomfort of the child. A tetanus convulsion is distinctly painful, and the increased tone of the muscles results in a debilitating discomfort. The giving of fluids to a child with tetanus is frequently necessary. If the child cannot swallow, the rectal or intravenous routes must be utilized. In order least to disturb the child with these procedures, it is important that he be well narcotized. Avertin has been found quite successful in accomplishing this purpose. The dosage most used was 80 mg. per kilogram of body weight, although in the future the larger dosage of 100 mg. per kilogram of body weight will be used. In the cases presented, after twenty minutes, avertin maintained a definite sedative action, often to the point of complete anesthesia for a period of five hours. There was a milder action for three or four hours longer. No nausea, vomiting or other bad effects from its use were encountered. One case of a child under its influence for thirteen days has been reported, without any evidence of harmful effects. Blood pressure readings were taken as a routine measure at frequent intervals while the child was under the influence of the drug. No serious disturbance was noted.

Dr. Harrison believes that the main value of avertin over many of the other sedatives in use is its more prolonged and more efficient action.

A NEW ORGANISM ASSOCIATED WITH MENINGITIS. DR. NOBLE P. SHERWOOD, Lawrence, Kan., and MARTHA EDWIN, A.B., and GEORGE MARTS, A.B., Kansas City, Mo.

The authors reported the study of a gram-negative, bipolar staining, acutely motile bacillus which was the sole organism present in the spinal fluid from a child with meningitis, who had been treated. Microscopically, the organism can easily be mistaken for the meningococcus, but culturally and in many other respects it resembles B. Whitmori. In male rabbits or guinea-pigs, when injected intravenously it produces an acutely ulcerative orchitis with very little systemic reaction, unless a fatal dose is administered. The organism is regarded by Bergy as a new pathogenic one. He has suggested that it be called Flavobacterium orchiditis.

DUBOIS ABSCESSES OF THE THYMUS IN AN INFANT AGED SIX AND ONE-HALF MONTHS. DR. R. KORITSCHONER, Kansas City, Mo.

The child was found dead in bed. Her history prior to this had been negative, and she was considered normal in every way. Autopsy showed an enlarged thymus,

weighing 32 Gm., from which a slightly hemorrhagic, creamy pus exuded. Sections revealed lymphatic hyperplasia. Death was caused by suffocation due to pressure on the trachea from an engorged thymus. The condition was nonsyphilitic, for streptococci were recovered from the thymus sequestrum.

ACUTE INFECTIVE AORTITIS. DR. F. C. NARR, Kansas City, Kan.

The specimen was from a boy, aged 7 years. He entered the hospital with a temperature of 101 F.; he was dyspneic and restless. A year before he had had pains and swelling of the joints. For these a tonsillectomy was done six months before admission. The symptoms returned two weeks before he entered the hospital following an otitis media. Death followed three days after admission. Autopsy revealed slight coarctation of the aorta at the site of the ductus arteriosus. There were two ulcerations proximal to the coarctation. There were a dissecting aneurysm, perforation of the aorta into the pericardial sac, acute pericarditis and hematopericardium. A postmortem blood culture showed Streptococcus infrequens (hemolytic). There were streptococci in the aortic wall at the site of the ulceration.

ILEOCECAL CYSTS: ETIOLOGIC FACTOR IN INTUSSUSCEPTION. DR. EDWIN LEE MILLER, Kansas City, Mo.

Ileocecal cysts are enterocystomas located in the ileocecal region. Twenty-four reports of cases of the condition have been recorded. The symptomatology of ileocecal cyst is the symptom of intestinal obstruction. The diagnosis of such a cyst has not been made prior to operation. Ileocecal cysts are developmental cysts; they are closely related to intestinal diverticulae.

The author reports a case affecting a 3 months old child who presented an intussusception which had been brought, about by the invagination of an ileal cyst through the ileocecal valve. The patient's temperature was 106 F. at the time of operation, three days after the first symptom. The deformity was reduced. An enterostomy was done, but the patient died. Necropsy demonstrated a small cystic tumor affecting the mesenteric border about 3 inches (7.6 cm.) above the ileocecal valve.

A summary of cases reported in the literature proves that the best treatment for ileocecal cysts that cause intussusception is complete resection of the invaginated bowel and cecum with immediate anastomosis between the small intestine and the transverse colon.

UNUSUAL CASE OF INTUSSUSCEPTION. DR. JOSEPH B. COWHERD, Kansas City, Mo.

The onset was at 2 weeks of age. The symptoms were mild at first, with gradually increasing severity to total obstruction, with the appearance of blood and a tumor mass. The patient had about six or seven attacks of total obstruction. The severity of the attacks gradually decreased, with complete disappearance. Operation was not allowed. A perfect recovery occurred at 1 year, and the child, who was presented, gave evidence of normal health.

CYST OF THE LARYNX IN INFANCY. DR. PHILIP S. ASTROWE, Kansas City, Mo.

A 4½ months old boy who had suffered from marked aphonia, intermittent cyanosis and stridulous breathing was presented. The symptoms noted during the first few days of life gradually increased in severity, causing every respiration to be audible at a distance. The marked retraction during respiration resulted in deformity of the chest. Cyanosis was more marked during excitement. The child could make no audible cry.

On laryngeal examination, a mass was found filling the entire left side of the glottic and subglottic space, the size of a pea. Incision of this mass yielded a clear yellow fluid with collapse of the walls. The symptoms were not relieved by this operation, so that tracheotomy had to be performed for the relief of

symptoms. Ten days later a laryngeal fissure was made in the median line, and it was deemed necessary to remove the vocal cords on the left side with a portion of the epiglottis.

Thereafter, the course was marked at first by general convulsions and difficulty in feeding the child because of the tracheotomy tube. Eventually, the tube was safely removed, and the voice returned; the stridor and cyanosis disappeared in about six weeks. This was followed by a steady, normal gain in weight.

REPORT OF PROGRESS FIVE YEARS AFTER THYROIDECTOMY AT TWO YEARS OF AGE. DR. DAMON O. WALTHALL, Kansas City, Mo.

The patient entered St. Luke's Hospital on Oct. 19, 1925. The parents stated that the child had been nervous and slightly underweight, with a fast pulse, a tumor in the neck and prominence of the eyes for approximately two years. One year previously she had become much more irritable and nervous, which symptoms had gradually become worse. The mother said that the child had not had any contagious disease or any other illnesses. As a baby, the feeding was breast milk; however, at this time the baby was restless at night and did not sleep well. On entering the hospital, the pulse rate was 150; the respiration rate, 20. On the day of operation, the pulse rate varied from 160 to 175, and the respiratory rate, from 30 to 40. The blood count showed: hemoglobin, 70; red cells, 4,280,000; white cells, 7,200; no differential count was made. The urine had a specific gravity of 1.010, an acid reaction and a negative reaction for albumin, sugar and bile; microscopically, there were from 3 to 6 pus cells per high power field. Occasionally, a red blood cell and a cast were found.

A subtotal thyroidectomy was performed by Dr. Hertzler on October 20. He described the gland as being a diffuse, fibrous, firm enlargement of both lobes and the isthmus of the thyroid gland. It was not nodular; each lobe was the size of a walnut, and the gland was very vascular and friable with few adhesions.

The patient made an uneventful recovery and was discharged from the hospital in a little over two weeks.

On Aug. 18, 1929, at the age of 7 years, the patient returned to St. Luke's Hospital for a tonsillectomy. The findings were very huge tonsils and adenoids in which there had been repeated attacks of tonsillitis and sore throat. At all times there was a great deal of secretion from the throat.

On entrance, the pulse rate was 90; the respiratory rate, 22. On the day of operation, the pulse rate varied from 130 to 140, and the respiratory rate, from 20 to 30. On the third day following tonsillectomy the patient went home from the hospital in good condition. On this entrance to the hospital, the laboratory findings in the urine were: specific gravity 1.020; acid reaction; negative for albumin, sugar and bile; acetone. Microscopically, a few bacteria and a few pus cells were seen in the high power field. The blood count showed: hemoglobin (Sahli), 85 per cent; red cells, 4,400,000; white cells, 6,800; coagulation time, three minutes and ten seconds.

Pathologic examination of the tonsils gave very large measurements. The crypt surfaces were dilated and everted, and on the cut section were quite hemorrhagic and contained several areas of cellular tissue.

A diagnosis of hyperplastic, ulcerated tonsils was made.

CARDIOSPASM IN THE NEW-BORN AND IN LATER INFANCY. DR. O. F. BRADFORD, Kansas City, Mo.

Dr. Bradford stated that he did not attempt to vouch for the accuracy of the term cardiospasm as an anatomic condition, but that he would cite briefly a few cases in which the clinical aspects together with the radiologic findings were sufficient for a diagnosis and the institution of rational treatment. Two types were shown. The first and less common of these presented the condition as an entity. In the second type, it coexisted and was apparently secondary to other pathologic conditions. Lantern slides were shown, and brief suggestions were made for treatment.

CONGENITAL TORTUOUS URETERS. DR. EDWIN H. SCHORER, Kansas City, Mo.

CASE 1.—A boy, aged 9 years, had been apparently well the first two years, although he could not be trained. When 26 months old, he began to have intermittent fever, at times as high as 103 F., but he was not clinically ill. This condition lasted six months. At first it was diagnosed as pyelitis, but later, as a markedly enlarged pelvis. Much dilated and tortuous ureters were found on both sides. The results of cystograms, pyelograms, phenolsulphonphthalein tests, examinations of the urine (cytologic and chemical) and examinations of the blood during the past seven years were given. The boy was presented; he was quite well and active. He did well at school.

The different opinions as to the course of events and the method of treatment to be followed were discussed.

CASE 2.—A boy, aged 2 months, had no kidney disturbance. He had congenital syphilis, otitis at 3½ months, pertussis at 5 months, a reaction to vaccination against smallpox at 12 months, impetigo at 15 months and tonsillitis at 17 months. When 18 months old, he voided frequently, but the urine was normal. When 19 months old, he refused to eat; he voided infrequently, but in very large quantities. At 35 months, a large tumor (kidney) was felt on the right side. The boy was under the care of a urologist, who resorted to the then known methods of diagnosis. It was then found that either kidney might be much enlarged at times, and a diagnosis of congenital bilateral hydronephrosis was made.

The boy was not seen for seven years; in fact, he was never really ill. He was seen a few hours before death due to pericarditis.

Autopsy showed hypertrophy and dilatation of the heart, acute fibrinous pericarditis and bilateral congenital hydronephrosis, without apparent obstruction of the ureters, and a chronic interstitial nephritis.

Discussion of the two cases as to the cause of the findings, prognosis and treatment was suggested.

ACUTE INFECTIOUS PURPURA HAEMORRHAGICA WITH CARDIAC COMPLICATION, DR. S. A. STADLER, Kansas City, Mo.

The patient was admitted to the Kansas City General Hospital on Aug. 12, 1927, with a condition diagnosed as purpura haemorrhagica.

The family history was unimportant.

The past history indicated that the patient had always been a healthy boy, having had the usual diseases of childhood without apparent complications. Adenotonsillectomy had been performed two years previous to the onset of the present illness.

The history of the onset revealed that less than twenty-four hours before the patient appeared at the hospital and while staying at a boys camp in the country, he complained of nausea and fatigue. Vomiting and chilliness rapidly followed, and soon afterward, a severe nasal hemorrhage, which could not be stopped with the means at hand. When increasing pallor and weakness were noted, the boy was rushed to the hospital.

On admission, examination showed a well developed and well nourished boy, aged 12, bleeding profusely from the nostrils and vomiting blood, and extremely weak, pale and restless; the pupils were dilated, and respiration was shallow and rapid. On the chest and back were several purple blotches in the skin, varying in size from that of a quarter to that of a silver dollar. On both legs were numerous infected insect bites, which formed sites for purpuric spots, some of which were crusted over, and blood escaped from beneath the crusts. Nasal examination was impossible on account of hemorrhage. The pupils were dilated, but reacted to light. The ears were normal. The mouth and throat were normal; the tonsils had been removed. Blood was seen dripping from the posterior nasopharynx. The lungs were normal . The apex of the heart slightly to the left, and the sounds were largely replaced by loud blowing murmurs, apparently hemic. The rhythm was good. The temperature was 97 F.; the pulse rate, 108, weak; the

respiration rate, 24. A blood count showed: red cells, 2,500,000; white cells, 27,600, with 90 per cent neutrophils and 210,000 platelets; the clotting time was six minutes.

The nasal hemorrhage seemed controllable only by manual pressure and only while the pressure was maintained, packs being of no avail. On account of the increasingly grave condition of the patient, it was decided to do an emergency blood transfusion, and after the patient had received 480 cc. of blood the hemorrhage subsided, the temperature rose, and the patient soon became restful. Twenty-four hours later, with a temperature of 104 F., a large quantity of bloody urine was voided, the nasal hemorrhage recurred; the patient was restless and delirious; the skin was moist, and a definite cadaveric odor was noted. A transfusion of 320 cc. of blood gave a prompt and favorable response as previously.

During the next ten days, the calcium, iron and hemostatics given to correct the condition of the blood seemed effective, but on the sixteenth day after admission the patient was suddenly near collapse, complaining of extreme pain and tenderness all over his abdomen; the temperature rose to 105.4 F., and soon copious bloody stools and a large amount of bloody urine were passed, with a recurrence of nasal hemorrhage. A transfusion of 480 cc. of blood immediately relieved the situation for a time, and in twenty-four hours, when a recurrence of hemorrhages was believed to be imminent another 320 cc. was given, with good results.

Progress seemed favorable for the next few days, and on the twenty-first day of hospitalization, the following points were noted on examination: The apex of the heart was three-fourths inch outside the midclavicular line; the right border was not displaced, and the aorta was not widened; the rhythm was irregular, interrupted by extrasystoles and premature beats; there were a presystolic murmur and a thrill at the apex, and a loud blowing murmur, systolic, best heard over the aortic area, but transmitted over the precordium and into the carotids. The blood pressure was 104 systolic and 80 diastolic. Blood counts typical for the resulting anemia showed gradual improvement, with a platelet count around 280,000, and hemoglobin of 60 per cent. The urine was normal.

The patient was discharged one month after admission to the hospital feeling quite well but anemic and with a mild cardiac insufficiency. He has since appeared at irregular intervals for examination and treatment, and a recent examination showed that there was an arrhythmia, with a mitral murmur; compensation was fair. The red blood cells numbered 3,500,000; the hemoglobin was 65 per cent.

Saturday Morning, Oct. 8, 1932

FRANK C. NEFF, M.D., *President, Presiding*

VIABLE MUSCLE IMPLANT FOR THE TREATMENT OF SIGMOID SINUS THROMBOPHLEBITIS IN CHILDREN. DR. O. JASON DIXON, Kansas City, Mo.

Since Zaufal in 1880 first opened the sigmoid sinus for the removal of an infected thrombus, gauze plugs have been used for the postoperative control of bleeding. These gauze plugs act as an infected foreign body and must be removed. Their removal presents a difficult problem: If they are removed too early, recurrence of hemorrhage and an expulsion of the newly formed thrombus occurs. If not removed early enough, they may play a part in the reinfection of the newly formed thrombus. Their removal always entails undesirable disturbances of an infected wound. They do not hasten the formation of the firm thrombus. When the noninfected sigmoid is accidently opened during mastoidectomy, the gauze plugs are especially undesirable, as they carry infection from an acutely infected field into a noninfected, open blood vessel.

To overcome these objectionable features, Dr. Dixon has used an inverted strip of the posterior half of the sternocleidomastoid muscle as a means for permanently occluding the open vessel. This muscle, with its freshly sectioned end,

hastens the formation of a firm thrombus when inserted into the opened sigmoid, remains in situ and retains its viability. It has its own independent and ample blood supply and plays no small part in the healing process of the injured vein. Only loose dressings within the wounds are necessary, and at no time does the wounded vein need to be redisturbed.

Experimental studies on the dogs have demonstrated the safe application of this procedure and also have indicated that the thrombosed vein becomes recanalized and the muscle remains viable.

Clinical cases and descriptive drawings of the procedure, as well as lantern slide demonstrations of the experimental studies on the dog, were shown.

EFFECT OF MALARIAL THERAPY ON PATIENTS WITH CONGENITAL SYPHILIS. DR. C. C. DENNIE, Kansas City, Mo.

Dr. Dennie described a family of seven children and presented the father and mother. All had cerebrospinal syphilis except the youngest. This child was born after the mother had received a thorough course of treatment before its birth. The blood and cerebrospinal fluid of this infant showed a negative serology.

Six children had positive findings of syphilis, both in the blood and in the spinal fluid. With the exception of the one next to the youngest child, they all received a course of arsphenamine, and bismuth was administered, followed by malaria (an average of ten chills each).

Following the malaria, negative reactions were found in the spinal fluid of the children who had received the malarial treatment. The fluid of the one who had not received the course of malaria remained positive.

ECZEMA DUE TO FOOD ODORS. DR. CHARLES J. ELDRIDGE, Kansas City, Mo.

The rôle of allergy is fairly well established in the etiology of certain types and cases. Little has been written, however, on the influence of food odors on the skin. Dermatologists recognize emanations (not pollen) of certain plants, e. g., primrose, as a cause of dermatitis. In certain cases, ivy poisoning breaks out when the patient is in proximity to this plant.

A patient with eczema, who gives positive cutaneous reactions to egg, was presented. The patient was kept in a strictly egg-free environment, and on numerous occasions exacerbations of the chronic eczema had developed when he was exposed to the odor of egg. Other similar cases of eczema due to egg have been observed. Because of the extreme sensitivity to egg, treatment has been limited to control of the diet and environment and to local applications. Spontaneous recovery is to be expected in most cases.

CONGENITAL ASPIRATION PNEUMONIA IN STILLBORN AND NEW-BORN INFANTS: AN ANALYSIS OF ONE HUNDRED AND FIFTY-NINE NECROPSY EXAMINATIONS. DR. FERDINAND C. HELWIG, Kansas City, Mo.

In a series of one hundred and fifty-nine necropsy examinations of stillborn and new-born infants dying in the first few hours of life, 41.5 per cent showed some degree of aspiration pneumonia, which, in the majority of instances, was considered to be an important factor in the death of the baby. The clinical records of the mothers were analyzed, and the gross and microscopic examination of most of the placentas, as well as histologic examination of the viscera of all the babies, was done as a routine measure. An analysis of these data showed that eclampsia, hypertension, cesarean section, maternal infection, toxemias, long automobile rides, premature separation of the placenta, complicating uterine myoma, version and extraction, forceps, strenuous mouth-to-mouth insufflation, dry labor, difficult posterior abnormalities of the cord, placental infarction, prolonged ether anesthesia and premature uterine contraction were possible factors which, in some instances, might have been partially responsible for the aspirations. Incidentally, in seven of the cases nothing could be found which appeared to have any bearing on the production of the pulmonary findings.

From the pathologic examination, an extensive purulent exudate was found in some stillborn babies who had never breathed and in other infants who had lived for only a few minutes. Concomitant subendothelial hemorrhages were present in most instances. In some of the lungs it was impossible to detect the pneumonia with the naked eye. In many cases the character of the exudate varied from amniotic fluid to a diffusely purulent exudate. In most instances, it did not seem, from the microscopic findings, that the amniotic fluid acted as an irritant. However, in those stillborn infants in whom pus was present in the exudate, it would appear that it may have been a factor to produce an irritation, particularly when considerable meconium was present in the fluid. In none of the lungs of stillborn infants did the purulent exudate contain organisms.

The placentas showed an insufficient degree of placentitis or noteworthy infarction in a sufficient number of cases to be considered as important in influencing intra-uterine aspiration. Trauma at birth may have been a factor in some instances, however, in influencing respiration, since complicating hemorrhages of the brain were present in some cases.

In conclusion, it would seem that the length of labor, the choice of an anesthetic, the high incidence of fetal aspiration following cesarean section and strenuous efforts at resuscitation were factors which might have been avoided in the handling of some of these infants.

In the treatment, Murphy has employed the Drinker respirator in a limited number of cases of asphyxia at birth, with considerable success.

VERTEBRAL BONE CHANGES IN HODGKIN'S DISEASE WITH DIFFERENTIATION FROM OTHER LESIONS OF THE SPINE. DR. I. H. LOCKWOOD, Kansas City, Mo.

Dr. Lockwood brought before the Society a case of Hodgkin's disease, in a boy whose first symptom was shingles and whose presenting symptom on admission was backache. At this time a roentgenogram revealed definite destruction of bone in the first four lumbar vertebrae, the ilium and the femora, although six months previously there had been no definite changes in these structures. Biopsy established the diagnosis of Hodgkin's disease. The course was one of increasing severity, with destruction of bone of the dorsal and lumbar vertebrae, ilium and femora, and involvement of the lymph nodes, lungs, liver and skeletal muscles.

Sections of bone showed few trabeculae, those present being quite regular in their outline; osteoclasts were not seen. The marrow contained practically no fat; there was a fibrous tissue reticulum, with mononuclear cells and giant cells of the Reed type.

Hodgkin's disease frequently produces widespread destruction of bone, the vertebrae perhaps being the bones most frequently attacked. Hodgkin's disease must be considered in cases presenting vertebral destruction, and must be differentiated from those of malignancy, tuberculosis, chondrodysplasia and intraspongy nuclear hernias.

ENDEMIC GOITER, HEREDITARY TYPE, WITH CYSTIC DEGENERATION AND CRETINISM. DR. L. P. ENGEL and DR. HUGH L. DWYER, Kansas City, Mo.

A report was made of a remarkable family in which the grandmother, mother and all four children had large cystic goiters. In addition to this, the youngest child was a cretin. The cretin and one other child were presented to the Society. It is known that thyroid secretion influences the retention of calcium, and that the excretion of calcium is markedly increased in exophthalmic goiter and diminished in myxedema. The patients were studied with a view of ascertaining (1) the calcium, phosphorus and nitrogen metabolism in cretinism; (2) the effect of thyroid medication on mineral metabolism, and (3) the difference between dwarfing in cretinism and in chondrodystrophy, and the possible relation between these conditions.

ACUTE INTERNAL HYDROCEPHALUS: ITS TREATMENT BY FREQUENT COMPLETE DRAINAGE; CASES SHOWING END-RESULTS. DR. H. C. BERGER, Kansas City, Mo.

Acute internal hydrocephalus is usually a self-limited condition (its onset and end cannot be controlled except rarely by surgical intervention). It must be diagnosed early, before injury to the brain tissue results. By maintaining a reasonably low intracranial pressure, during the active process, injury of the brain is largely prevented, and a normal child is the result when the process has stopped. Certain signs indicate the time for drainage. Drainage must be done whenever pressure signs become manifest. To be most effective, this drainage must be complete (at times cisternal punctures have been effective, and later may be again, probably owing to temporary block in the spinal canal about the fifth cervical segment).

A number of these cases were presented to demonstrate the success of this method of handling hydrocephalus.

NEUROGENIC INCONTINENCE AND RETENTION IN CHILDREN. DR. CLINTON K. SMITH, Kansas City, Mo.

Dr. Smith reported a study of thirteen cases of dysfunction of the bladder of neurogenic origin in children. The diagnosis and management, including surgical measures for the correction of the difficulty, were discussed. Lantern slides were shown.

DEMONSTRATION OF CORRECTIVE EXERCISES IN SPEECH DEFECTS. DR. E. T. GIBSON, Kansas City, Mo.

Cases of speech defect are part of the regular inflow of the neurologic clinic and dispensary. As the patients come in, they are divided into two classes. One type of case is called "stuttering," which is practically always psychologic. It is looked on as a psychoneurosis, and the patients should be treated by ordinary methods of psychotherapy rather than by any mechanical training, although that may be added. Cases of congenital aphasia and some injuries sustained at birth are occasionally seen. The second group, of course, is the one in which more patients have become candidates for mechanical training.

ERYTHRODERMIE CONGÉNITALE ICHTHYOSIFORME. DR. S. PAKULA, Kansas City, Mo.

Dr. Pakula described a new type of dermatosis, which has not previously been described, in an adolescent boy. The patient presented a generalized erythroderma on which was superimposed an ichthyosis hystrix. The lesions were circumscribed patches or spinous excrescences in which papular or verrucous elements entered into their formation, involving the entire trunk, legs, back and, to a slight extent, the face.

The case differed from others in the literature chiefly in its clinical characteristics as follows: It was not a nevus type, in that the lesion could be picked off without leaving a bleeding surface; it had a wide distribution; it was a papular growth not previously described.

A discussion of the case, with photographs before beginning treatment and its termination, the treatment and results and photomicrographs, with a discussion of the pathology, were presented.

Book Reviews

Skin Diseases and Nutrition. By Erich Urbach. Price, $7. Pp. 242. Vienna: Wilhelm Maudrich, 1932.

This book on an important subject is the first of its kind that the reviewer has ever seen. The first part of the book consists of articles on chemical properties of the skin and the influence of nutrition on these properties. These are exhaustively considered from every standpoint, and there is a wealth of reference to the literature. Then there is a chapter on cutaneous diseases due to malnutrition. The author considers these diseases extensively and well. The next chapter is on diseases of the skin due to alimentary infections and intoxications, and then one on dermatoses caused by diseases of the digestive tract, etc. In other words, in the first part of the book the author considers the subject from the standpoint of nutrition and the cause and relation between nutritional disturbances of all sorts and the dermatologic diseases. In the special part of the book, there is an extensive list of the diseases of the skin with their dietetic treatments, together with case histories illustrating the same and samples of diet.

There is an extensive consideration of allergy. As demonstrating the soundness of the author's views, the following may be quoted in speaking of cutaneous or intracutaneous reactions as tests for nutritive allergen. "I believe that it is worse than worthless and positively misleading to draw any definite conclusions from the outcome of these reactions." Again, in speaking of the dietetic treatment of infectious eczema, he says "There is no such thing as a complete diet for eczema, but it behooves us to study out the dietary errors and probably form a nutritive allergen. Furthermore, it is our duty to alter metabolism in the sense of correcting a constitutional inferiority."

It is too bad that typographic errors are to be found in so many instances. These do not mar the book, which is well printed and well illustrated, but they do somewhat detract from the general impression.

Nervous Disorder in Infancy and Childhood. By N. Hobhouse. Price, 8 shillings, 6 pence. Pp. 207, with 4 illustrations. London: H. K. Lewis & Co., Ltd., 1932.

This book was written primarily for practitioners and interns. The nervous disorders of infancy and childhood are discussed from a purely practical point of view. An attempt has been made to consider more completely those disorders which are ordinarily accorded very little space in the standard textbooks, such as, hyperkinesia, disorders of speech and articulation and the management of cerebral palsies. The common neurologic diseases about which a great deal has been written in the past are discussed briefly, but the fundamental principles are well covered. The prognosis of each condition is thoroughly presented, and the treatment and management that can be undertaken by the practitioner are completely discussed. Very little space is devoted to pathologic changes.

The first part of the book includes injuries sustained at birth, cranial abnormalities, inflammatory diseases of the nervous system, abiotrophies, myopathies and convulsions. The latter half of the publication is composed of chapters on focal lesions of the brain, diseases of the peripheral nerves and psychic and behavior problems in children.

This book should be especially valuable to busy physicians who are chiefly interested in treatment and who desire to bring their knowledge of nervous disorders of children up to date in a short time.

Le kala-azar infantile. By Dr. Paul Giraud. Price, 30 francs. Pp. 79, with 12 illustrations and 1 colored plate. Paris: Gaston Doin, 1932.

In this monograph Dr. Giraud presents in an excellent manner his study of kala-azar occurring in infants of the Mediterranean countries. The author bases his statements on his own personal experience with eighty-six cases of this disease, as well as on the observations of other outstanding workers in this field. The entire subject is covered completely and systematically. The epidemiology is considered first, followed by a clinical study which reveals an intimate knowledge of the manifestations of the illness. Prognostic signs and diagnostic procedures are discussed in detail. The pathologic anatomy of kala-azar was written in collaboration with Dr. Claudiére. Treatment with the salts of antimony and other adjuvant measures is described thoroughly and practically. The reading of this valuable monograph by all physicians practicing in countries where kala-azar occurs would undoubtedly cause more widespread recognition and diagnosis, as well as better results in treatment. Among the patients treated by the author, 71 per cent were cured.

L'epilepsie chez l'enfant et le caractère épileptoïde. By Dr. Gilbert-Robin. Price, 18 francs. Pp. 146. Paris: Gaston Doin, 1932.

After long experience observing and studying epileptic children, the author describes in detail his conception of the constitution and attributes of these patients. He states that it is possible to diagnose the condition by the child's conduct and character even before the occurrence of convulsions, loss of consciousness or vertigo. Epileptoid tendencies are suggested by the occurrence of psychic retardation, obnubilation, impulsiveness, uncontrollable anger, cruelty, lapses in writing, antisocial reactions, obstinacy and disturbances in sleep. The occurrence of these traits and actions is illustrated by numerous case histories in which the behavior of the children is fully described. Among the hereditary factors considered to be of importance are alcoholism, syphilis and psychopathic disorders. One chapter is devoted to a discussion of the various methods of treatment employed in epilepsy. This book represents a careful and extensive clinical analysis of the intellectual and psychic manifestations of epileptic children, and by picturing the epileptoid behavior pattern it should aid in establishing early diagnosis and treatment.

A Suggestion for an Experimental Attempt at Local Immunization in Poliomyelitis Through Irradiation of the Portals of Entry. By S. Peskind. Price, $1. Pp. 15. Cleveland: Mount Printing Company, 1932.

The author states that he has obtained rapid local immunization in the treatment of large numbers of patients with focal infection by focal irradiation with ultraviolet rays. He suggests the possibility that if local immunity could be increased sufficiently, the poliomyelitis virus could be destroyed at its portal of entry into the body and prevented from reaching the nervous system. To test this theory, a series of experiments on monkeys is suggested, such as the administration of poliomyelitis virus followed by exposure to ultraviolet rays.

The author apparently has profound confidence in the ability of ultraviolet rays to arrest infectious processes, even deep infections, when the rays are applied to the skin. The arguments for means of increasing local resistance are unconvincing.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.
Place: London. Time: July 20-23, 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.
Place: London. Time: May 26, 1933.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Washington, D. C. Time: May 8-10, 1933.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: New York. Time: May 6, 1933.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. M. Hines Roberts, Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

Medical Society of State of New York

Chairman: Dr. Brewster Doust, 605 Medical Arts Bldg., Syracuse.
Secretary: Dr. G. C. Sincerbeaux, 6 William St., Auburn.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

TEXAS PEDIATRIC SOCIETY

President: Dr. Boyd Reading, 2201 Avenue D, Galveston.
Secretary-Treasurer: Dr. F. W. Hoehn, 1006 Medical Arts Bldg., Waco.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. St. George Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Edward L. Benjamin, 2021 Grand Concourse, New York.
Secretary: Dr. Harry M. Schapiro, 1882 Grand Concourse.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Every Second Wednesday of each month, except June, July, August and September. Annual meeting, May 10, 1933.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

DALLAS COUNTY PEDIATRIC SOCIETY

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. John Caffey, 50 Haven Ave., New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelphia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.